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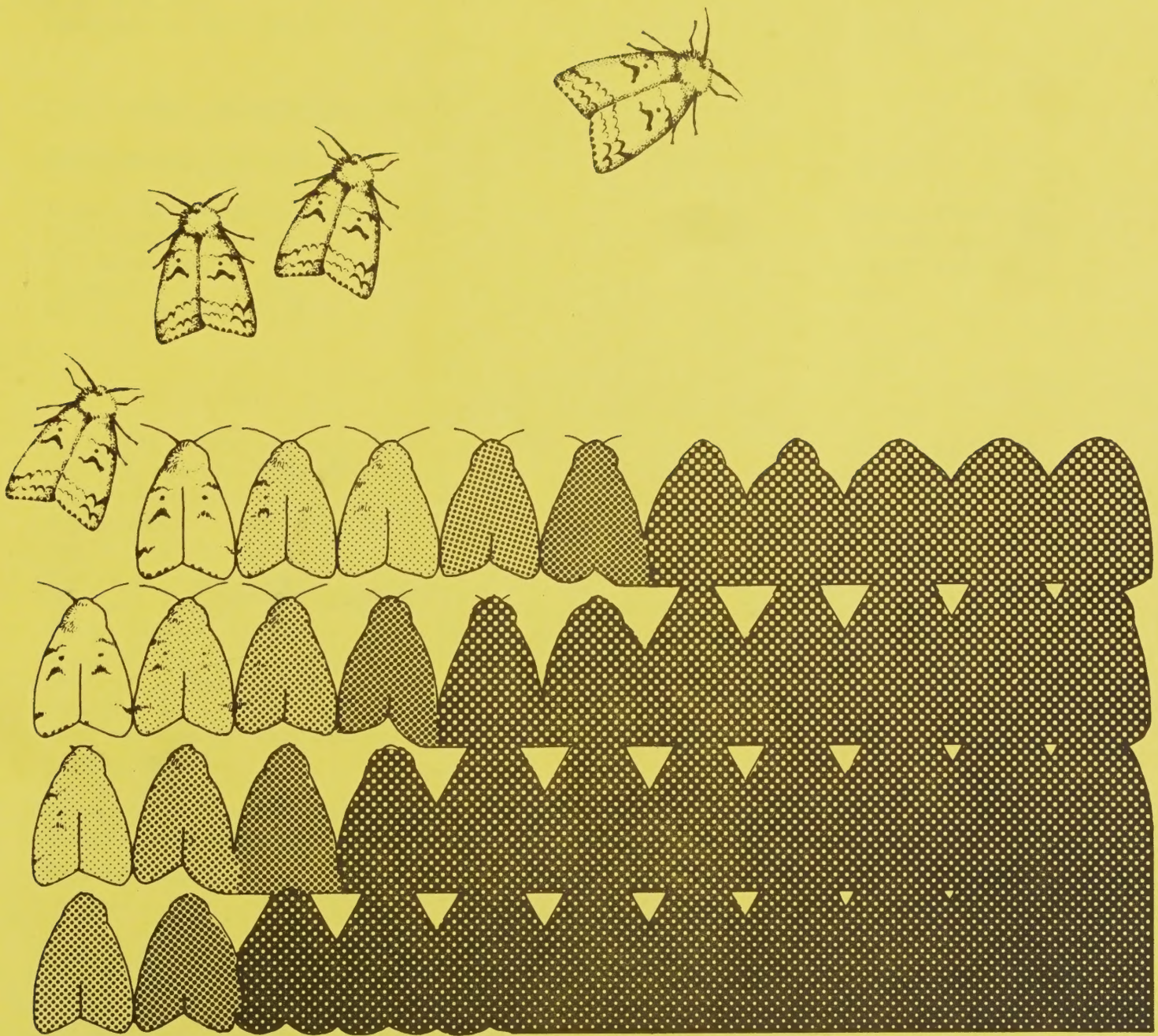
Gypsy Moth Suppression and Eradication Projects

Draft Addendum to the Final Environmental Impact Statement as Supplemented – 1985



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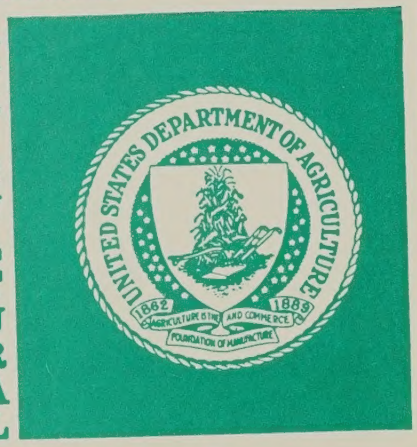

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Draft Addendum to the Final Environmental Impact Statement on Gypsy Moth Suppression and Eradication Projects in the United States as Supplemented – 1985

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Abstract: This document provides a plain language version of the worst case analysis in the Final Environmental Impact Statement (Final EIS) on Gypsy Moth Suppression and Eradication Projects in the United States as supplemented. The Final EIS was approved on March 8, 1985. Since that date, the United States District Court for the District of Oregon, in Oregon Environmental Council v. Kunzman (Civil No. 82-504-RE), ruled that although the main text of the Final EIS was legally adequate, the worst case analysis in Appendix F failed to meet the regulatory requirement for clarity. In response to this ruling, the Forest Service and the Animal and Plant Health Inspection Service have prepared this addendum. The bulk of this Draft Addendum is a plain language version of Appendix F. In addition, toxicity data and cancer risk calculations have been clarified to make the risks more understandable.

Comments concerning the Draft Addendum or its relationship to the Final EIS should be sent to the following address and must be received by December 4, 1985 .

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Introduction

On April 26, 1985, the United States District Court of Oregon ruled that the Final Environmental Impact Statement for Gypsy Moth Suppression and Eradication Projects, as supplemented - 1985 (FEIS), was legally adequate but that the worst case analysis was not understandable by its intended readers. In making this ruling the Court found that although the worst case analysis in Appendix F of the FEIS contained all the necessary information, it was too technical, complex, and full of equations and calculations. This document responds to the Court's ruling.

The bulk of this document is a plain language version of Appendix F. This version is contained in Appendix H. It translates the technical data contained in Appendix F into terms that disclose possible human health problems in language that all readers can understand. The rest of this document includes the following information in Appendix I:

(1) A verbal description of the toxicity tests summarized in Tables 1 through 7 in Appendix F. This description is included to clarify the basis for setting the no observed effect levels (NOEL's) used in the worst case analysis. It also provides the descriptive background needed to identify possible health effects resulting from exposure to insecticides used to control the gypsy moth.

(2) Clarification and recalculation of the cancer potency and risk of N-nitrosocarbaryl.

(3) Clarification of the cancer potency and risk of 4-chloroaniline, a breakdown product of diflubenzuron.

(4) Clarification of cumulative effects that could result from being exposed to both eradication and suppression projects in a lifetime.

(5) Possible contamination of diflubenzuron with dioxin.

(6) An errata sheet correcting typographical errors in references.

Since this document does not propose substantial changes in the proposed action or contain substantial new information, the Forest Service and the Animal Plant Health Inspection Service (APHIS) do not consider it to be a supplement under the National Environmental Policy Act regulations. This document only contains information that was presented to the U.S. District Court to clarify issues about human health risk and the plain language version of Appendix F.

Although this document is not considered a supplement, it is being sent for review and comment by agencies, organizations, and individuals listed in Appendix B of the FEIS to further public involvement in the decision-making process. Comments regarding the material in this document will be considered and published as a final addendum to the FEIS. The administrators of the Forest Service and APHIS will review and consider this final document along with the FEIS before issuing a record of decision on the alternative selected for cooperative gypsy moth suppression or eradication projects.

Appendix H
Plain Language Summary of the Health Risk Analysis

OVERVIEW

Four chemical insecticides are being considered for use in projects to suppress or eradicate gypsy moths. Appendix F analyzed the risk to human health of using each of these insecticides. In doing so, it was necessary to use scientific methods, terms, and formulas. Without such scientific rigor, it would be hard, if not impossible, for other specialists to judge whether the conclusions are correct.

This appendix, however, is for the general reader. It presents the methods and results of the risk analysis in words that can be understood by decision-makers and the public. The difference between these two appendixes is the level of detail--not the level of accuracy. Readers who want to check the math or see what studies were used should refer to Appendix F.

Conclusions

The four chemicals being considered for use in gypsy moth projects are acephate, carbaryl, diflubenzuron, and trichlorfon. The basic question being asked in the risk analysis is, Would human health be affected by their use? Briefly, the answer is as follows:

- All realistic doses to the general public from routine spraying would be at levels deemed safe by the Environmental Protection Agency or the World Health Organization.

- All exposures from routine operations would be below levels that could cause birth defects in the general population.

- With two possible exceptions, realistic doses to workers from routine operations would have no ill effects. Where there are effects, they likely would be minor and would not last long. Symptoms might include mild dizziness, headaches, or eye irritation.

- About half the estimated doses from abnormally high exposures (worst case doses) in routine operations would be above the safe levels. At the most, there would be less than 1 chance in 500 of such a high exposure. Again, the effects (if any) would be minor.

- In most cases, aircraft spills would have no lasting effects on human health.

- The most severe effects could come from truck spills. Symptoms could range from nausea to shortness of breath to death. With prompt medical help, most symptoms can be reversed. Moreover, the odds of a truck spill occurring are very low. A truck spill probably would occur less than once for every 100 million acres treated. (That is about 250 times the number of acres that have been treated each year in the past.)

- The odds of a person getting cancer from routine operations would be no higher than 4 in a million. This is about the same risk as smoking 8 cigarettes in an entire lifetime. In most cases, the odds would be much lower.

- The total added risk of cancer from routine operations would be about 0.05 incidences per year in the exposed population of 5.4 million people. This is based on the amounts that have been sprayed in the past.

- It seems extremely unlikely that spraying projects would result in mutations that could be passed to offspring.

Method

These conclusions were reached by using a three-step process used in most risk analyses:

(1) Hazard Identification--What are the toxic (poisonous) properties of each of the insecticides? What doses are deemed safe for humans? What doses might cause harm?

Most of this information comes from laboratory tests that use mammals. Other sources include studies of human poisonings and research involving other organisms.

(2) Exposure Analysis--Who is likely to be exposed to the insecticide as a result of spraying? How much of the insecticide is likely to enter their bodies? How often will they be exposed?

People can be exposed in several ways and can take in different amounts of the chemicals. The exposure analysis describes ways in which people might be exposed. These situations, called "scenarios," range from properly handled routine operations, through the worst cases that could occur during routine applications, to accidental spills of chemical concentrates.

Since these scenarios cover a wide range of possible exposures, any real life exposure should be close to or less than these.

(3) Risk Evaluation--How will human health likely be affected by actual spraying operations?

This is answered by comparing the results of the first two steps. That is, the estimated doses (the amounts that might enter people's bodies) in the different exposure scenarios are compared with the doses found to be safe or harmful to health.

Use of Worst Case Assumptions

Whenever there is doubt about what might happen when the chemicals are used, this analysis assumes the worst. For instance, where there is doubt that a chemical can cause cancer, this analysis makes the worst case assumption that it can. Another example is that all standard application rates are increased by 10 percent to account for normal variations in preparing and spraying the chemicals. In the worst case scenarios, these rates are doubled to account for possible major errors in mixing and spraying. It is also assumed that a person might eat fruit or vegetables that have been sprayed, even though spraying is done before the growing season for most fruit and vegetables. Further, the amount of food in an exposed person's diet is assumed to be greater than it is in the average diet.

Together, the worst case assumptions help ensure that health risks will not be understated. But in doing so, they probably suggest that the spraying projects pose greater risks than are likely. In other words, the risks listed above probably are exaggerated. For example, use of worst case assumptions suggests that there is a small risk of cancer occurring. Yet there is no evidence that any of the four chemicals have caused cancer in humans at any dose levels.

The following sections discuss the methods and conclusions of the health risk analysis in greater detail.

HAZARD IDENTIFICATION

Determining Toxicity

The first step in the risk analysis is to determine the toxicity of each of the four chemicals. Toxicity is the ability of a substance to harm health.

All four chemicals have been studied in the laboratory using conventional toxicity tests on animals. It is standard practice in the health field to use the results of

such tests to help determine the hazards to people. This is because different animals, including humans, often react similarly when given the same dose of a substance. But this is not always the case. For example, dogs seem much more sensitive than other mammals to carbaryl. Therefore, good judgment and care must be used when applying the results of animal tests to humans.

Health effects caused by toxic chemicals fall into two groups: threshold responses and nonthreshold responses. Most obvious effects seem to fall into the first group, which can include birth defects, nervous disorders, and many other ailments. Cancer and mutations fall into the second group. But it is not the types of diseases that separate the two groups. Rather, it is the way in which the responses occur.

With threshold responses, there is a certain amount of the substance that can enter the bodies of most animals or humans without causing any harm. The dividing line between doses that have no effects and those that do is called the threshold level. Once the threshold is crossed, increased doses will increase the intensity and extent of the effects. In theory at least, these types of responses are fairly predictable and similar in all healthy people.

Nonthreshold responses work differently. With nonthreshold responses, any dose might set off a reaction, but there is no certainty that it will do so. There will be an adverse effect only if the chemical successfully invades the body and reaches certain strategic points, such as the DNA in human cells. It is possible for a large dose of the substance to enter a person's body without any effect at all. But the greater the lifetime dose, the greater the odds of seeing these effects.

Threshold Responses

Animals and people do not show threshold responses until certain doses are exceeded. Therefore, to assess health risks from a substance, it would seem necessary to find out its threshold dose. That is, how much of the chemical will the body tolerate before there are ill effects? But this threshold dose cannot be known precisely without running a seemingly endless series of tests using slightly different doses. So toxicologists instead look at the dose-response relationship and focus on the highest doses that are known to cause no ill effects. These are called no-observed-effect levels (NOEL's).

No-observed-effect levels for chemicals are determined in standard, controlled laboratory tests. In these tests, a

population of animals (such as mice of roughly the same age) is separated into groups. Each group then is given a different daily dose of the substance for an extended period of time. The highest dose that has no apparent adverse effects is the NOEL.

To compare doses given to different species or different sized animals, a common unit is needed for measuring doses. Sometimes doses are based on body weight. At other times, they are based on the surface area of the body. In this study, doses are expressed as fractions of body weight. The standard unit is milligrams (of chemical) per kilogram (of body weight). One kilogram is equal to 2.2 pounds, while a milligram weighs a million times less. When the dose is given daily, as is the case with most NOEL's, the unit is milligrams per kilogram per day (mg/kg/day).

There may be several NOEL's for each chemical--both for different species and different responses. While different species of mammals, including humans, tend to respond similarly when they are given the same dose of a chemical, they do not respond identically. Furthermore, toxicity tests often look for specific types of responses (such as birth defects) and might overlook others. Figure H-1 shows a hypothetical example of a substance with several NOEL's. This hazard analysis always focuses on the lowest NOEL to make sure that risks will not be understated.

As suggested by Figure H-1, once the dose of a substance exceeds the NOEL and crosses the threshold, the effects tend to increase as the dose increases. The increase in effects can take two forms: an increase in intensity (such as increasing kidney problems), or the addition of new types of effects (for example, birth defects in addition to kidney problems). The first effects might be relatively mild and, even then, result only after long-term exposure. But as the dose increases, the effects would become more severe.

The most severe effect from a toxic substance is death, with the most extreme effect being death from a single (acute) exposure. The one-time or short-term dose that kills 50 percent of a group of treated lab animals is called the LD_{50} (for "lethal dose, 50 percent"). An oral LD_{50} is the lethal dose from swallowing a substance. A dermal LD_{50} is the lethal dose on unbroken skin. Clearly, a person would be at great risk if exposed to a substance at a level near or above its LD_{50}.

Because of biological differences between test animals and humans, NOEL's cannot be responsibly applied to humans without using a safety factor. That is, to err on the side of caution, NOEL's derived from animal studies usually are

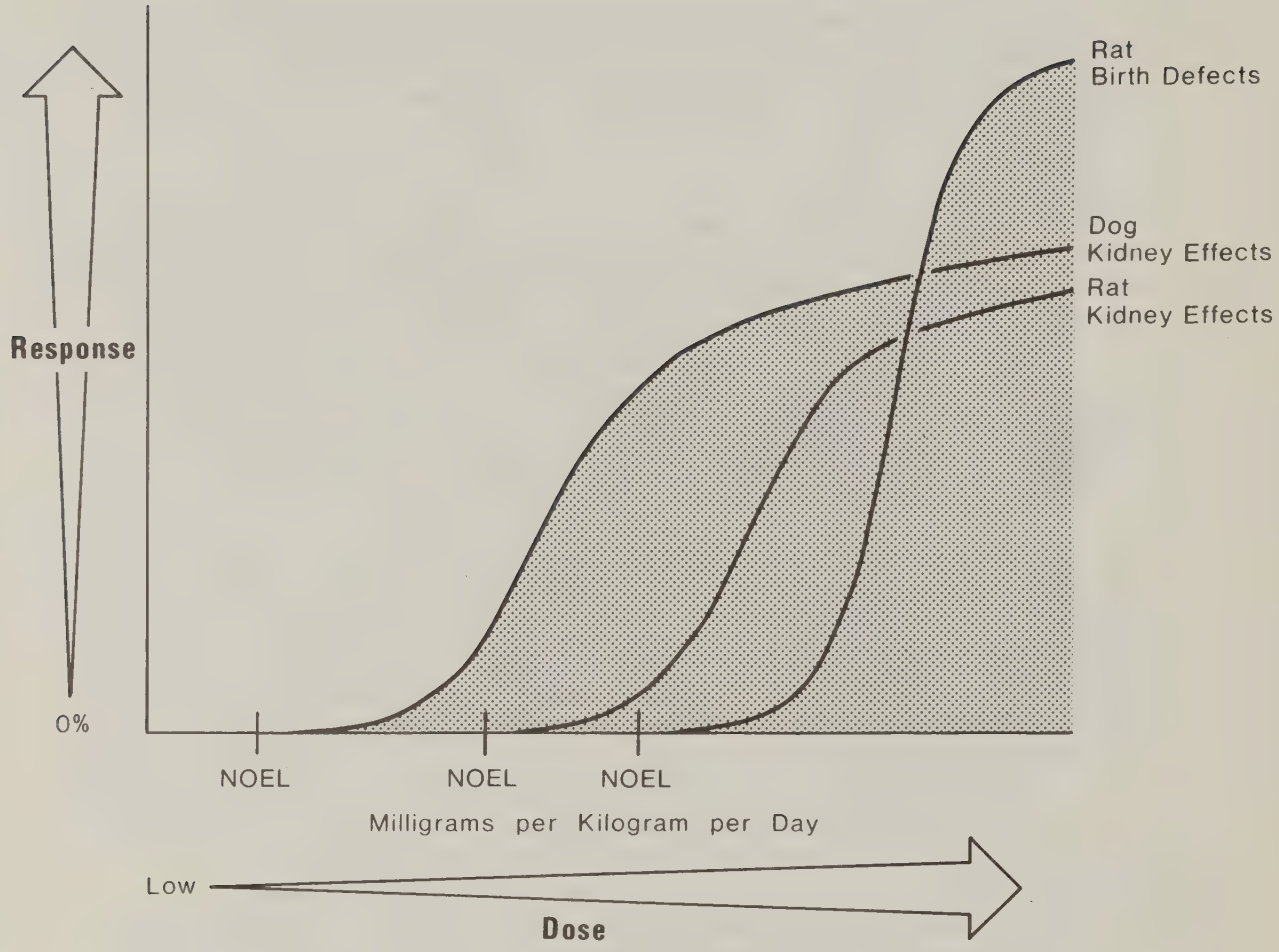

Figure H-1.--Typical dose-response pattern for threshold responses. This example shows a chemical with three no-observed-effect levels (NOEL's). The lowest NOEL is for kidney effects in dogs. The intensity of this effect increases as the dose increases. Even larger doses could result in birth defects in addition to kidney problems. (The two NOEL's for kidney effects show how one species might be more sensitive than another to the same chemical.)

reduced by a safety factor to set safe doses for humans. The most common safety factor is 100, but it can range from 10 to 1,000. The U.S. Environmental Protection Agency (EPA) and the World Health Organization both use safety factors to establish safe doses for various chemicals. For each chemical, the safety factor that they use depends on how sure they are that the available studies can be applied to humans. The term they use for the safe dose is "acceptable daily intake (ADI)." The ADI is believed to be the maximum dose of the chemical that can be taken every day over a person's lifetime without any adverse effects. Figure H-2 shows the relationship between NOEL's, ADI's, and LD_{50}'s.

LD_{50} - Acute lethal dose. One-time or short-term dose that is lethal to 50 percent of treated animals.

Threshold - Long-term dose level at which adverse effects first occur.

NOEL - No-observed-effect level. Long-term dose that does not result in apparent adverse effects in test animals.

Safety Factor - Factor applied to lowest NOEL to set safe lifetime dose to humans.

ADI - Acceptable daily intake. Maximum dose that a person could safely take every day throughout lifetime without harm to health.

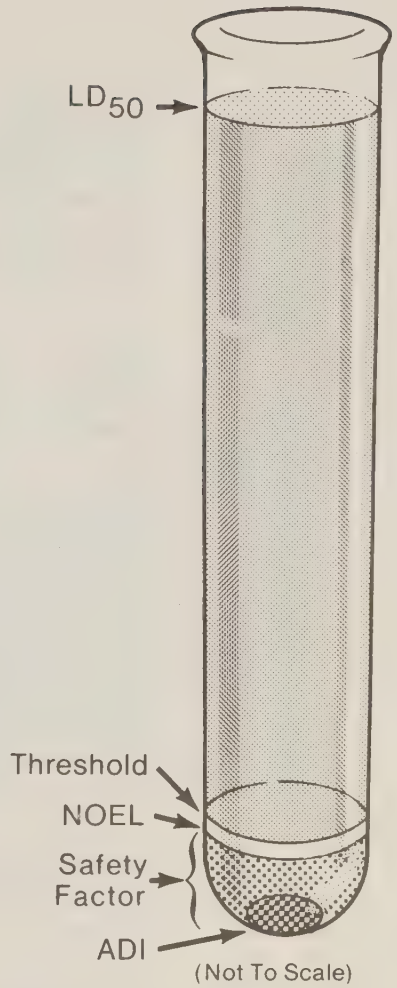

Figure H-2.--Relationship between benchmark doses seen in laboratory tests and established safe doses for humans.

ADI's serve as starting points for evaluating the health risks associated with using chemicals. If the exposure analysis shows that the expected dose to humans will be less than the ADI, then the dose is considered safe for most people. For those doses that are above the ADI, it is necessary to look more closely at the data about the chemicals. Specifically, it is necessary to determine the margin of safety--that is, to see how close the dose is to the various NOEL's. It is also necessary to look at the type of responses that might be involved. If the expected dose occurred every day for a long period and approached the NOEL for a response that is not easily cured, then the safety margin would be small and the health risk might be great. In such situations, a responsible decision-maker would want a high margin of safety before using the chemical.

It must be kept in mind that the NOEL's used in this analysis are from studies that involve daily exposure over a long time. Also, ADI's are considered to be doses that can be taken safely every day for an entire lifetime. Yet most potential exposures from gypsy moth projects are

one-time or short-term exposures. Therefore, comparing the estimated exposures to ADI's and NOEL's might not give a true picture of the risks involved. The error always would be on the side of overstating the risks.

Nonthreshold Responses

Scientists do not all agree about the link between human exposure to chemicals and the occurrence of mutations or cancer. But generally it is thought that no threshold levels are involved.

Doctors usually do not speak of degrees of cancer; a person either has cancer or does not. The chance of getting cancer has been compared to the chance of being hit by a car when crossing a road blindfolded. Even if there is only one car within 100 miles, there is a small chance it will hit. If there are two cars, the chances will be greater, and so on. Likewise, the odds of getting cancer from a known carcinogen (cancer-causing substance) increase with the size and duration of the dose.

Hazard assessments for cancer have two steps. The first is to see if there is evidence showing that the chemical in question could cause cancer. The second is to figure out the odds of getting cancer from different doses. Since there are no known cases of human cancer being caused by any of the four chemicals being considered, data on animals were used. Where tests indicated that a chemical might cause cancer in mammals, a mathematical model was used to determine its cancer potency.

Various models (or formulas) can be used to determine cancer potency. For this study, a linear model was used. The linear model assumes that a steady increase in dose will result in a steady increase in the odds of getting cancer. This model is overly simplistic, but it usually errs on the side of overstating the chances of cancer occurring.

The linear model also assumes that a given total dose will have the same effect no matter what the dosing period is. For example, a large dose given on 1 day is assumed to have the same effect as the same total dose given in smaller amounts over several days. However, this may not always be the case. So this assumption puts some uncertainty into the risk analysis.

An example of the assumed linear relationship between a dose of a specific substance and the chance of cancer is shown in Figure H-3. To show how the linear model overstates the effects of low doses, the graph includes a curve that is closer to known cancer potencies.

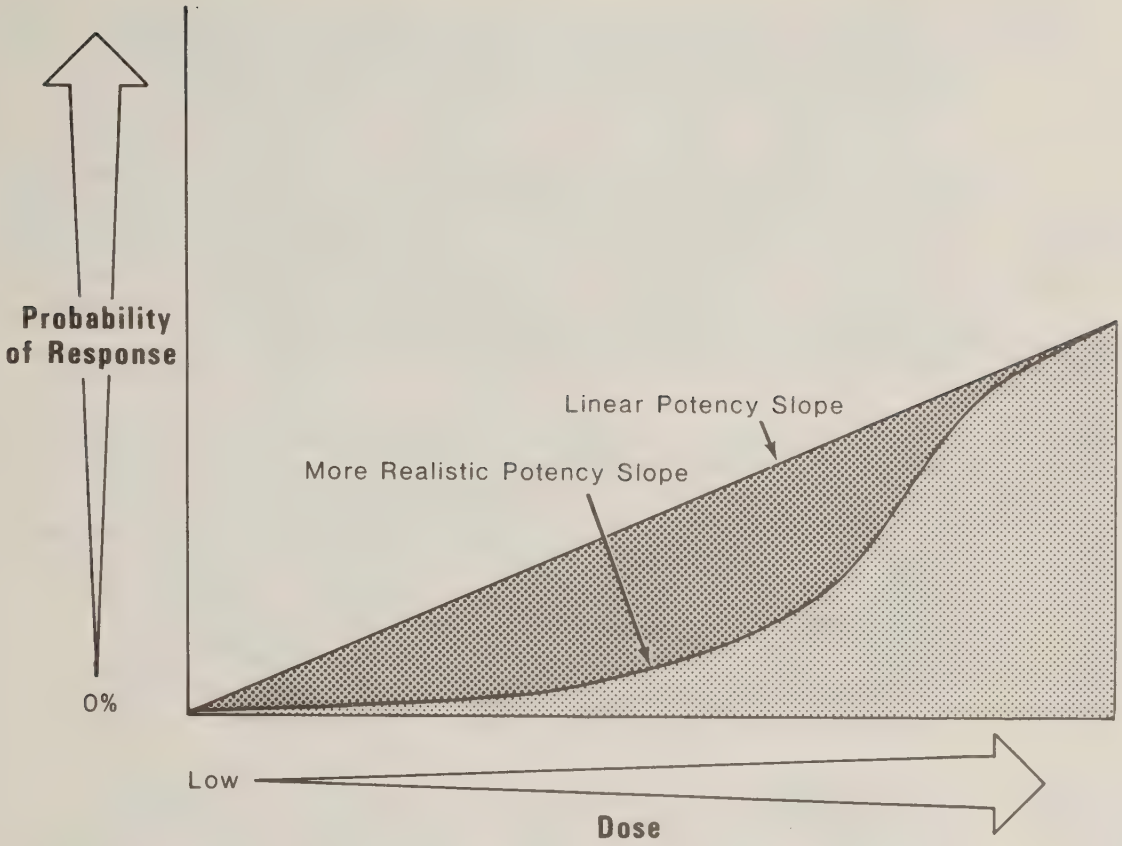

Figure H-3.--Relationship between dose and probability of cancer assumed in linear model. The curved line represents a more realistic potency slope. The shaded area suggests how the linear model overstates the effects of low doses.

The straight-line slope in Figure H-3 represents cancer potency. It shows what the increase in cancer probability is for each increase in dose. If the slope were steeper, then the cancer potency would be greater. The potency slope also can be expressed as a number; the higher the number, the more potent the carcinogen. Because potency slopes and values can be difficult to grasp, this summary also indicates what daily dose of each chemical would result in a 50-percent chance of getting cancer from that chemical. These numbers help compare the potency of the chemicals and are new ways of expressing the data already in Appendix F.

Cancer is the end result of a multi-step process that starts with mutations (changes) in body cells. Changes in most body cells might lead to cancer. But changes in most cells cannot be inherited by offspring. Cells involved in reproduction--called germ cells--are another matter.

Mutations in these cells can be inherited. Some of these changes may be minor, but others can be quite serious.

At this time, there are no generally accepted mathematical models for determining the risk of mutations. Instead, scientists weigh the evidence from various laboratory tests to try to assess the ability of a chemical to cause mutations in humans. Such a "qualitative" picture is incomplete; it indicates whether the chemical can cause heritable mutations (those that can be passed to offspring), but it cannot quantify the risks for humans.

However, it may be safe to assume that the risk of heritable mutations would be no greater than the risk of cancer. Cancer and heritable mutations often seem to start in the same way. The main difference is that substances that cause cancer have many more possible targets in the body. While cancer is caused by changes in any cell, heritable mutations are caused only by changes in germ cells. Thus, use of the linear cancer model (which overstates the risk of cancer) to estimate the risk of heritable mutations would grossly overestimate such risks.

Hazard Levels of the Four Insecticides

All the insecticides under consideration are currently registered by the Environmental Protection Agency for the control of gypsy moth larvae. This means that, in EPA's judgment, available studies indicate that none of these chemicals will cause unreasonable adverse effects in people or the environment when properly used.

The acceptable daily intakes, lowest known no-observed-effect levels, acute lethal doses, and 50-percent cancer probability doses, are compared in Table H-1. The higher the number, the less harmful the chemical. The table also shows the cancer potencies of the four chemicals. For cancer potency, the higher the number, the more harmful the chemical in terms of cancer. The following subsections summarize the toxic properties of each chemical. (More detailed information can be found on pages 42 to 67 of the FEIS, on pages F-12 to F-22 of Appendix F, and in Appendix I.)

Acephate

Based on the effects of large, one-time doses, acephate is considered to be a moderately toxic insecticide. Its main health effect is to reduce the level of cholinesterase, an enzyme found in red blood cells, blood plasma, and elsewhere and that is essential to the functioning of the nervous system. If this enzyme cannot be produced (called "cholinesterase inhibition"), a number of ill health effects

Table H-1.--Comparison of lowest no-observed-effect levels, acceptable daily intakes, acute lethal doses, and cancer potencies of the four insecticides.

Benchmark	Acephate	Carbaryl	Diflubenzuron	Trichlorfon
	Milligrams per kilogram of body weight			
Dermal LD_{50}	10,000[a]	9,600[a]	2,000[a]	2,100[a]
	Milligrams per kilogram of body weight per day			
Lowest NOEL	0.25	3.125	1.1[a]	1.0
ADI	0.025	0.1	0.011	0.01
50% Cancer Probability[b]	20	3,800[c]	26[d]	110
	Per milligram per kilogram per day over a lifetime			
Cancer Potency	0.025	0.057[c]	0.019[d]	0.0047

[a]Highest dose tested; actual number would be higher.
[b]Lifetime daily dose that would result in a 50-percent chance of person getting cancer from this chemical alone.
[c]Carbaryl itself is considered to be noncarcinogenic; the potency value is for N-nitrosocarbaryl, while the 50-percent probability figure is for the amount of carbaryl required to form enough N-nitrosocarbaryl to pose a 50-percent chance of cancer. As discussed in footnote 1 on page H-13, the cancer potency of N-nitrosocarbaryl could range from 0.057 to 3.6. If the higher potency value were used, the 50-percent probability figure would be 61 mg/kg/day.
[d]Diflubenzuron itself is considered to be noncarcinogenic; statistic is for 4-chloroaniline.

can occur. The lowest NOEL's, which are for cholinesterase inhibition in rats and dogs, are 0.25 milligrams per kilogram of body weight per day.

There is no evidence that acephate causes birth defects. However, it can cause maternal toxicity. Symptoms in lab animals have included increased incidences of abortion. The NOEL for maternal toxicity is more than 10 times higher than the lowest NOEL for this chemical. EPA has established the ADI for acephate at 0.025 milligrams per kilogram of

body weight per day. This means that the highest "safe dose" for a person weighing 154 pounds (70 kilograms) is 1.75 milligrams per day.

Acephate can cause gene mutations in cells grown in the laboratory. But these effects occur only at dose levels that are so high that they cannot be tolerated by mammals.

It is uncertain if acephate can cause cancer. But acephate is suspect since it has caused tumors in female mice at very high dose levels in lab tests. Therefore, this analysis makes the worst case assumption that acephate can cause cancer. Assuming this, and using the linear model, acephate's cancer potency for humans is 0.025. This means that a person would have to receive 20 milligrams of acephate per kilogram of body weight every day throughout his or her life to have a 50-percent chance of getting cancer from that chemical alone. For a 154-pound person, that would be 1.4 grams (0.05 ounce) per day.

Carbaryl

Carbaryl is also considered to be a moderately toxic insecticide. In addition to animal studies, its effects on humans have been documented in poisoning incidents, worker exposure studies, and volunteer ingestion studies. The laboratory tests have revealed such symptoms as reduced cholinesterase, swelling of kidney cells, and various birth defects in animals exposed during gestation.

The Environmental Protection Agency used a NOEL of 10 milligrams per kilogram per day as the basis for setting carbaryl's ADI. This NOEL is for cholinesterase inhibition in rats. With one exception, birth defect NOEL's for other mammals are much higher. EPA applied a safety factor of 100 to the rat NOEL to set the ADI for carbaryl at 0.1 milligram per kilogram per day. For a 154-pound person, this "safe dose" would be 7 milligrams per day.

Based on the weight of the evidence, EPA concluded that carbaryl will not cause birth defects in humans. Further, there has been one study to see if actual exposure to carbaryl has led to birth defects in people. That study found no link between the two. But because of public concern about birth defects, the analyses for this EIS used the lowest known birth defect NOEL. That NOEL is lower than the one used by EPA and is 3.125 milligrams per kilogram per day. The birth defects showed up in dogs at doses ranging from 6.25 to 50 milligrams per kilogram per day.

It may be that the results of carbaryl studies using dogs should not be applied to humans. Those studies suggest

that dogs might be much more sensitive than other mammals to this chemical. Because of these doubts, EPA has called for more data about how carbaryl affects dogs.

While the evidence is not conclusive, carbaryl seems to have a weak ability to cause mutations but no ability to cause cancer. But there is concern that carbaryl could combine with nitrites to form N-nitrosocarbaryl, a compound that can cause mutations and cancer. Such a chemical reaction can take place only under acidic conditions like those found in the human stomach. The N-nitrosocarbaryl produced would pose a cancer risk only if it could last long enough in the stomach to cause tumors. It is uncertain that N-nitrosocarbaryl could last that long.

In one study, carbaryl and nitrite were fed directly to rats, but no tumors were observed even at doses that caused acute poisoning. Even so, this analysis makes the worst case assumption that carbaryl would be converted to N-nitrosocarbaryl in the human stomach. Based on a review of the literature and use of the linear model, the cancer potency of N-nitrosocarbaryl was found to be 0.057. This means that a dose of 8.8 milligrams of N-nitrosocarbaryl per kilogram of body weight every day during a person's lifetime could result in a 50-percent chance of that person getting cancer. To get that much N-nitrosocarbaryl, a 154-pound person would have to take in about 260 grams of carbaryl daily.[1]

Diflubenzuron

Diflubenzuron is selective in its toxicity. It causes the outside skeleton of insects to rupture when they molt. It is considered to be only slightly toxic to humans. There is no evidence that diflubenzuron causes birth defects. The main health concern is that diflubenzuron is known to raise the level of sulfhemoglobin and methemoglobin in blood. This effect could impair the blood stream's ability to carry oxygen. The lowest NOEL, 1.1 milligrams per kilogram per day, is for this type of response. EPA has set

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[1]As discussed in court during Oregon Environmental Council v. Kunzman, the cancer potency of N-nitroso-carbaryl could range from 0.057 to 3.6 depending on what study is used to calculate the potency. If the higher potency value were used, a 154-pound person would have to ingest 4.2 grams of carbaryl every day to have a 50-percent chance of getting cancer. This range of potency values is discussed further in Appendix I.

the ADI at 0.011 milligrams per kilogram per day. For a 154-pound person, this "safe dose" would be 0.77 milligrams per day.

Laboratory studies indicate that diflubenzuron does not cause mutations or cancer. But there might be some risk of cancer associated with exposure to this chemical because one of its breakdown products--4-chloroaniline--might cause cancer. The evidence about 4-chloroaniline is suggestive, not conclusive. Nonetheless, this analysis makes the worst case assumption that 4-chloroaniline can cause cancer in humans. Using the linear model, the cancer potency was found to be 0.019. A 154-pound man would have to be exposed to about 1.8 grams of 4-chloroaniline per day throughout his life to have a 50-percent chance of getting cancer from this chemical. For diflubenzuron to be the source of this exposure, something like the following would need to occur: Every day of his life, the man would have to eat an entire fish that had been exposed to 5 grams of diflubenzuron.

Trichlorfon

Trichlorfon is a moderately toxic insecticide. Its lowest NOEL is 1.25 milligrams per kilogram per day for reduced levels of cholinesterase in dogs. At considerably higher doses, lab animals have shown some changes in their immune systems and had birth defects. The immune system NOEL is 20 milligrams per kilogram per day and is from a study that used rats. The lowest birth defect NOEL also is from a rat study. This NOEL is 8 milligrams per kilogram per day, which was the highest dose tested. A study using hamsters found no birth defects at doses 25 times higher than that. The World Health Organization has set trichlorfon's ADI at 0.01 milligram per kilogram per day. For a 154-pound person, this "safe dose" would be 0.7 milligrams per day.

For this analysis, it must be assumed that trichlorfon could cause genetic mutations and cancer in humans. While tests using whole animals have been inconclusive, laboratory studies using bacteria, yeast, and mammalian cells indicate that trichlorfon is mutagenic. And while there is no direct evidence that trichlorfon can cause cancer, it is necessary to assume that it can because of the similar ways in which cancer and mutations form. Making this worst case assumption and using the linear model, the cancer potency would be 0.0047. This means that a 154-pound person would have to be exposed to about 7.4 grams of trichlorfon every day for a lifetime to have a 50-percent chance of getting cancer from this chemical.

EXPOSURE ANALYSIS

For an insecticide to cause harm to a person, two conditions must be met. First, the substance must be in the person's environment. Second, it must enter the body.

Exposure to an insecticide must come from the air that a person breathes, or it must be in water that the person drinks, or in food that will be eaten, or it must come into contact with the skin. The amount of chemical in a person's environment is the exposure level.

If the chemical is in the air, it can enter the body through the air passages and lungs (called the inhalation route). If it is on a person's clothes or skin, it must pass through the skin to enter the body (the dermal route). A chemical also could get into the body if the person eats food or drinks water that has insecticide residues (the ingestion, oral, or dietary route). The total amount that actually enters the body is called the dose.

In gypsy moth projects, two groups of people can be exposed. The first group is workers. This group includes supervisors, pilots, truck drivers, mixer/loaders, and observers (including inspectors, scouts, rangers, and ecologists). The second group that could be exposed includes members of the general public living in or near sprayed areas.

To find out how much of the substance these groups could be exposed to, all likely ways a person could be exposed were identified. Then doses from these routes of exposure were estimated using standard methods and assumptions. These doses are used in the risk evaluation section, along with information from the hazard identification section, to assess the health risks to workers and the public from exposure to the insecticides.

Possible Routes of Exposure

To cover most ways that a person could be exposed, a set of situations, called scenarios, is used. These range from situations that possibly could occur during routine spraying operations to an event that is very unlikely, such as accidental spills.

Exposures from Routine Spraying Operations

Workers and the public can be exposed to the insecticides in two ways: directly or indirectly. Direct exposures result from the chemical coming into contact with the skin or breathing in the spray. (As discussed on page F-34 of Appendix F, inhalation exposures from spraying operations are insignificant.) Thus, observers who happen to be under the spray plane or mixer/loaders who splash some of the

chemical on their hands would get direct exposures. Direct exposure also can come from spray drift. Indirect exposures result from touching sprayed things like yard furniture or tools that have residues on them. Indirect exposures also can come from eating meat or vegetables or drinking water that have insecticide residues. Figures H-4 and H-5 illustrate possible routes of exposure from routine operations. Table H-2 describes the routes of exposure for the scenarios for routine operations.

Exposures from Accidents

The highest exposures to workers and residents could come from large amounts of insecticide that are accidentally spilled from an aircraft (an airplane or helicopter) or a truck. If the mixture is spilled onto a person, the primary route of exposure would be through the skin. If it

Figure H-4.--Possible routes of exposure to workers from routine gypsy moth control projects.

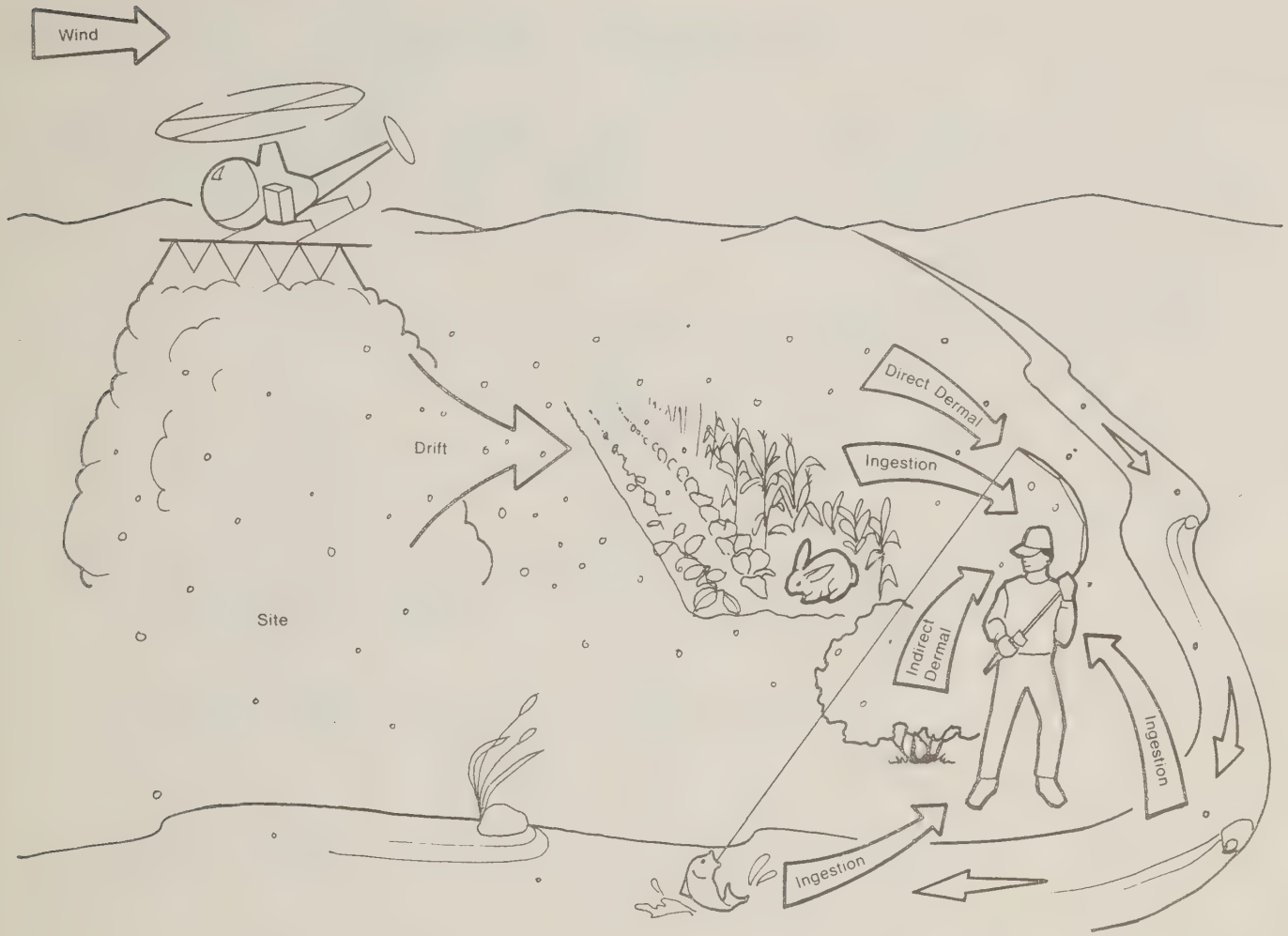

Figure H-5.--Possible routes of exposure to the general public from routine gypsy moth control projects.

is spilled into a stream or other water body, the route would be by drinking water or eating fish from that stream. Possible routes of exposure from accidents are shown in Figure H-6. Table H-3 describes the routes of exposure for the accident scenarios.

Estimating Doses

For each chemical in each scenario, a range of doses was obtained. Realistic doses reflect levels that might realistically occur during routine spraying operations. Worst case doses are very high estimates of the most a person would get for that scenario. These exposures are based on assumptions that fit the real world (that is, that are plausible) but that always overestimate risk. Certain actions, such as warning people of spraying operations and making sure that spraying takes place only under the right weather conditions, would reduce the likelihood of worst case doses.

Table H-2.--Possible routes of exposure for routine operation scenarios

Exposure Scenario	Routes of Exposure
Workers	
Mixer/loaders	All routes of exposure (dermal, inhalation, and ingestion).
Observers	All routes of exposure.
General Public	
Direct	Dermal and inhalation exposure from being outside during a spray operation plus dermal exposure from contact with things like plants, grass, or outdoor furniture.
Indirect	No direct dermal exposure (person is inside during spraying) but indirect exposure from contact with items that have insecticide residues.
Dietary	Ingestion exposure from eating about a pound of fish, a pound of rabbit, a pound of goat, and a pound of vegetables or fruits, and drinking about a half gallon of water--all of which have insecticide residues.

Most of the doses in this assessment are based on actual field studies where carbaryl was used in spraying operations. These studies provide a range of dose levels that actually occurred to both workers and residents during spraying operations that are similar to gypsy moth spraying operations. Because the insecticides are all applied in a similar way and the routes of exposure are expected to be similar for all four chemicals, the carbaryl studies are the best source available for estimating doses in this analysis. Nevertheless, there are some uncertainties in using this method because the four chemicals have different properties. For example, the amount of time it takes for the chemicals to break down, or degrade, varies. In addition, the amount of chemical on the skin that will be absorbed into the body (called the dermal absorption rate) varies.

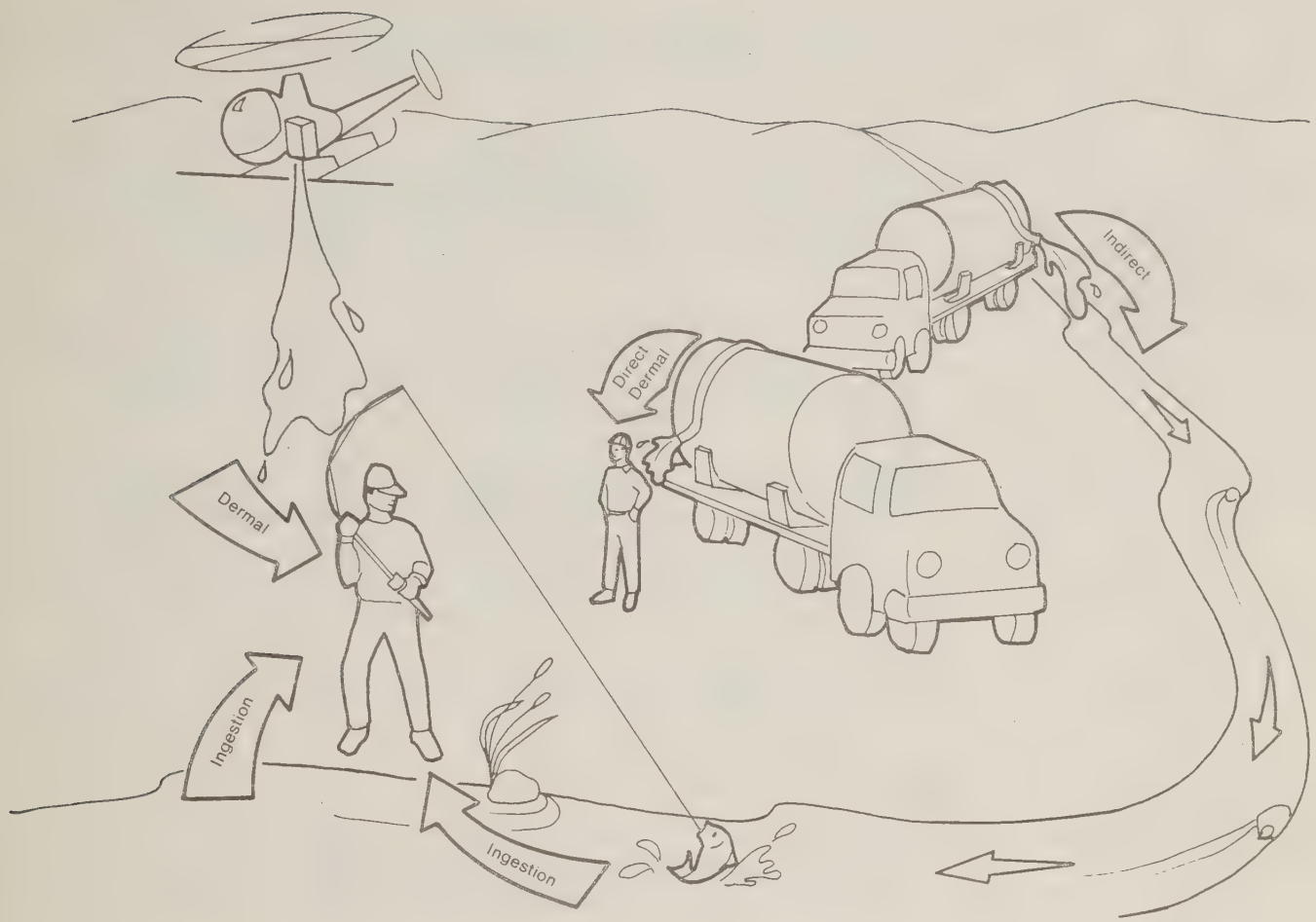

Figure H-6.--Possible routes of exposure from accidents.

Thus, in extrapolating the doses in the studies to the four chemicals discussed here, these differences must be considered. For example, a 10-percent dermal absorption rate is used for all four chemicals even though the estimated absorption rates for each of the chemicals are lower than this. In this way, no risks are underestimated. The varying degradation rates are also taken into account when determining lifetime doses. The application rate (the amount of active ingredient of chemical applied per acre) is also a consideration in determining doses. The application rate for both trichlorfon and for carbaryl is 1.0 pound per acre. The application rate for acephate is 0.75 pound of active ingredient per acre, and for diflubenzuron, 0.06 pound per acre.

Table H-3.--Possible routes of exposure for accident scenarios

Exposure Scenario	Routes of Exposure
Aircraft Spill	
Partial Dermal	Dermal exposure from the spill of a load of insecticide on a person that enters the body only through those areas not covered by clothes.
Full Dermal	Dermal exposure from aircraft spill that enters the body through exposed skin plus through soaked clothes.
Drinking Water	Ingestion exposure from drinking a half gallon of water from a stream where an aircraft spilled 300 gallons.
Eating Fish	Dietary exposure from eating a pound of fish from the site of a 300-gallon spill.
Truck Spill	
Dermal	Dermal exposure from a truck spill that results in 1 gallon of chemical on the skin.
Drinking Water	Drinking a half gallon of water from a stream that had 2,000 gallons of insecticide mixture spilled into it.
Eating Fish	Eating a pound of fish from a stream in which 2,000 gallons of insecticide had been spilled.

Once the basic dose for each chemical in each scenario was calculated, it was adjusted to account for variations in mixing and applications. "Realistic" doses are multiplied by 1.1 to account for normal variations that can increase doses. "Worst case" doses are multiplied by 2.0 to account for abnormal variations that can create major differences in the amount of spray being deposited. For more detail on mixing and application variations, see pages F-45 through F-47 of Appendix F.

The estimated realistic and worst case doses for all exposure scenarios are shown in Tables H-4 and H-5.

Table H-4.--Estimated realistic doses for exposure scenarios
(milligrams per kilogram per day)

Exposure Scenario	Acephate	Carbaryl	Diflubenzuron	Trichlorfon
ROUTINE OPERATIONS				
Workers				
Mixer/loaders	0.035	0.046	0.0028	0.046
Observers	0.0017	0.0022	0.00013	0.0022
General Public				
Direct	0.0017	0.0022	0.00013	0.0022
Drift	0.0011	0.0014	0.000087	0.0014
Indirect	0.00033	0.00044	0.000026	0.00044
Direct plus Dietary	0.025	0.012	0.00072	0.012
Indirect plus Dietary	0.024	0.0098	0.00061	0.0098
Observer plus Dietary	0.026	0.012	0.00072	0.012
Dietary only	0.024	0.0094	0.00059	0.0094
ACCIDENTS				
Aircraft spill				
Dermal (partial)	60	120	2.3	60
Dermal (full)	120	260	3.5	120
Drinking water	0.033	0.077	0.0015	0.033
Eating fish			0.00014[a]	
Truck spill				
Dermal	11,000	27,000[b]	430	11,000[b]
Drinking water	0.25	0.60	0.01	0.23
Eating fish			0.00091[a]	

[a]Dose is from 4-chloroaniline, a breakdown product of diflubenzuron
[b]The variation factor is not applied. These chemicals are premixed and there is no possibility for mixing error.

Table H-5.--Estimated worst case doses for exposure scenarios
(milligrams per kilogram per day)

Exposure Scenario	Acephate	Carbaryl	Diflubenzuron	Trichlorfon
ROUTINE OPERATIONS				
Workers				
Mixer/loaders	0.15	0.20	0.012	0.2
Observers	0.044	0.058	0.0035	0.058
General Public				
Direct	0.0075	0.010	0.0006	0.010
Drift	0.0049	0.0054	0.00032	0.0054
Indirect	0.0014	0.0018	0.00011	0.0018
Direct plus Dietary	0.11	0.12	0.0079	0.13
Indirect plus Dietary	0.11	0.12	0.0074	0.12
Observer plus Dietary	0.15	0.17	0.01	0.17
Dietary only	0.10	0.12	0.0073	0.12
ACCIDENTS				
Aircraft spill				
Dermal (partial)	110	230	4.2	110
Dermal (full)	220	470	6.4	220
Drinking water	0.060	0.140	0.0028	0.06
Eating fish			0.00025[a]	
Truck spill				
Dermal	19,000	27,000[b]	780	10,000[b]
Drinking water	0.45	0.60	0.018	0.23
Eating fish			0.0017[a]	

[a]Dose is from 4-chloroaniline, a breakdown product of diflubenzuron.
[b]The variation factor is not applied. These chemicals are premixed and there is no possibility for mixing error.

Doses from Routine Operations

Table H-6 summarizes how the realistic and worst case doses were estimated for each scenario for routine operations. (Pages F-27 through F-43 in Appendix F provide specific details about how these doses were determined.) All doses to the public overestimate risk because, in calculating these initial doses, it is assumed that the chemicals do not degrade (or decline) at all. Thus, the doses for each scenario are the highest that could be expected.

Unlike the other routine scenarios, the dietary dose is not based on the carbaryl studies. This dose is calculated based on residue levels of the insecticides found in meat, fish, vegetables, and water. To receive the multiple exposures under the dietary scenario, a person would have to gather and eat the food or drink the water right after the spraying.

The likelihood that people would get doses from eating vegetables or fruits with insecticide residues is very low. Gypsy moth spraying is done during the spring--when no fruit and very few vegetables are growing. But to ensure that even such a remote possibility is considered, doses from this source of food are included in the dietary dose. Realistic and worst case doses from residues in vegetables and fruits were based on studies on residue levels from the insecticides used in agriculture.

To determine the highest cumulative doses a person could get from all sources, some doses were combined. For example, the dietary dose was added to the direct, indirect, and observer doses to show the most the general public could be exposed to during routine operations.

Doses from Accidents

If an aircraft or truck spilled insecticide, workers and the general public could be exposed to much more than they would under routine circumstances. However, such accidents are rare. (The probabilities of accidents occurring, which are based on State and Forest Service records of such events, are discussed in more detail in the risk evaluation section.) A detailed discussion of the assumptions and methods used to determine accidental doses are on pages F-52 through F-55 of Appendix F.

Aircraft Spills. For aircraft spills, doses are calculated for dermal exposure and for drinking water and eating fish that have insecticide residues. The size of the load dumped is assumed to be 300 gallons. This is the size of the load typically used in gypsy moth spraying. This load could spill over land or into water. Exposures are based

Table H-6.--Methods for estimating doses from routine operations

Scenario	Realistic Dose	Worst Case Dose
Workers		
Mixer/loader	Based on urine levels in mixer/loaders from carbaryl studies. High range (not average) used.	Based on highest dose level (from urine) from carbaryl studies, as well as studies on other pesticides.
Observer	Based on dose level (from urine) in observers in carbaryl studies.	Assumes observer sprayed directly on 2 square feet of exposed skin.
General Public		
Direct	Based on average exposure levels for residents found in carbaryl studies.	Based on highest exposure level to residents reported in the carbaryl studies.
Drift	Dermal dose based on drift found offsite in a number of relevant studies; two-thirds of the amount deposited onsite gets offsite under routine assumptions.	Dermal dose based on two-thirds of amount deposited onsite under worst case assumptions (for example, application rate is multiplied by 2).
Indirect	Based on lowest dose found for observers in carbaryl studies.	Based on highest dose found for observers in carbaryl studies
Dietary	The estimated dietary exposure level is the sum of the following: eating a pound of meat (from two sources), fish, and vegetables and drinking a half gallon of water--all of which have insecticide residues.	
	Goat/Rabbit--Goats and rabbits are exposed through both dermal and inhalation routes.	Goats and rabbits are exposed to very high levels of insecticide.
	Fish--Based on residue levels found in actual field test of water intentionally directly sprayed with carbaryl.	Based on direct application to stream 6 inches deep with no dilution.
	Vegetables--Based on the low range of residue data from agricultural applications assuming vegetables are picked and eaten the same day as treatment.	Based on high range of residue data from agriculture applications.
	Water--Concentration in water calculated by the same method as for fish residues.	

on the assumptions that the spill over land hit a person or the person drank water or ate fish that the chemical spilled into.

Truck Spills. For spills from trucks, doses were calculated for dermal exposures and for drinking water or eating fish containing insecticide residue. Because no studies are available on exposures to workers from a truck spill, basic dermal doses were based on the assumption that a mixer/loader is exposed to 1 gallon of diluted insecticide in a day. The basic dose from drinking water containing insecticide residue was calculated in the same

way as for the aircraft spill. Doses from eating fish (exposure to 4-chloroaniline) are a portion of the amount of diflubenzuron in the fish.

Lifetime Exposures and Doses

To determine the risks of long-term health effects such as cancer from exposure to the four chemicals, it is necessary to know how much of the chemical a person might get in a lifetime. For the linear cancer model (described in the hazard identification section), the total lifetime dose must be expressed in terms of average daily dose. The average lifetime daily realistic and worst case doses are summarized in Table H-7.

Routine Operations

To figure the lifetime doses from routine spraying, the following information is needed:

- The length of the lifetime, assumed to be 70 years
- The type and number of gypsy moth projects that could take place in the same area during a lifetime
- The number of days the insecticides might be sprayed during each of those projects
- The amount of chemical a person could be exposed to during each of those days
- The length of time the insecticide remains in meat, on vegetables, or in water (called persistence)

Persistence is considered only in determining lifetime doses (not in determining initial doses). Lifetime doses are based on all the doses a person could get during the time it takes for the chemical to degrade.

The types of spraying projects generally used to control gypsy moths are eradication and suppression projects. Eradication projects are used in areas of the country where the gypsy moth has been established by artificial means. For example, a mobile home can carry the insect into a new area where it becomes established. Suppression projects usually are conducted only in areas where the gypsy moth is firmly established and spreads naturally.

For eradication projects, it is assumed that the insecticides may be sprayed as many as three times over a 6-week period. It also is assumed that the gypsy moth could be artificially introduced into the same area twice during the 70 years. Thus, in a lifetime, a person living in the same place could be exposed six times from eradication projects.

Table H-7.--Average lifetime daily doses for realistic and worst case exposures from eradication and suppression projects (milligrams per kilogram per day)

	Eradication Projects (6 exposures)		Suppression Projects (10 exposures)		Combined Eradication & Suppression Projects (16 exposures)	
Exposure Scenario	Realistic	Worst Case	Realistic	Worst Case	Realistic	Worst Case
Acephate						
Direct plus Dietary	0.000058	0.00018	0.000097	0.00031	0.00016	0.00049
Observer plus Dietary	0.000058	0.00027	0.000097	0.00045	0.00016	0.00072
Carbaryl (N-nitrosocarbaryl)						
Dietary	0.000000036	0.00000045	0.000000059	0.00000074	0.000000095	0.00000119
Diflubenzuron (4-chloroaniline)						
Dietary (eating fish)	0.000000068	0.0000014	0.00000011	0.0000023	0.000000079	0.0000037
Trichlorfon						
Direct plus Dietary	0.000017	0.00020	0.000028	0.00033	0.000045	0.00053
Observer plus Dietary	0.000017	0.00021	0.000028	0.00035	0.000045	0.00056

It is assumed that the chemical is sprayed only once in each suppression project and that such a project could be conducted in the same area every 7 years. Thus, a person would be exposed 10 times from suppression projects over 70 years.

Because the gypsy moth spreads naturally and can become established in new areas, suppression projects could be conducted in areas that previously received eradication treatments. If so, a person could get as many as 16 exposures in a lifetime (6 for eradication projects and 10 for suppression projects). A detailed discussion of how average lifetime doses are determined is on pages F-70 through F-86 of Appendix F.)

Carbaryl (N-nitrosocarbaryl). Carbaryl does not cause cancer. However, there is some concern that nitrite ions and carbaryl might react to produce N-nitrosocarbaryl, which can cause cancer. Because the probability of this taking place is unknown, it was assumed that it does. In humans, this reaction could occur only in the stomach, so the only dose that needs to be considered is the dietary dose.

The total dietary dose of carbaryl is the sum of the doses that a person could get during the time the substance remains, or persists, in food sources (meat and vegetables) or water. Carbaryl residues drop to zero in 7 days in meat, in 14 days in vegetables, and in 4 days in water. The analysis used the longest period (14 days) to ensure that the total dose was not understated.

The total doses of carbaryl are translated into N-nitrosocarbaryl doses. To get the average liftime dose, the total dose over the 2-week period is then multiplied by either 6 or 10 (the number of projects in a lifetime) and then divided by the number of days in a lifetime.

Acephate and Trichlorfon. For acephate and trichlorfon, the average lifetime doses were calculated for the two highest combined exposures. The first includes direct exposure to the insecticide during spraying and eating eat food and drinking water having residues (the direct plus dietary exposure scenario). The second includes an initial direct exposure to insecticide during spraying, as well as additional exposures to residues in food and water (the observer plus dietary exposure scenario).

The average lifetime doses for acephate and trichlorfon are based on the first dose from the spraying and the secondary exposures to residues in food and water. For acephate, the period required for residues to degrade is 20 days in both the realistic and worst case. For realistic doses from

trichlorfon, it takes 2 weeks for the residues to degrade completely. For worst case doses, it takes 60 days for the chemical to degrade. The total doses are then calculated just as they are for carbaryl.

Diflubenzuron (4-chloroaniline). Studies show that diflubenzuron does not cause cancer. But, it is not known for sure whether a breakdown product of diflubenzuron, 4-chloroaniline, can cause cancer. Because of this uncertainty, it is assumed that 4-chloroaniline can cause cancer. The risk of cancer would come from eating meat or fish, where 4-chloroaniline can be concentrated. Because fish would have the highest level of residues from the chemical, only realistic and worst case doses from eating fish are calculated.

The doses of 4-chloroaniline are figured as a percentage of the estimated doses of diflubenzuron. The residues of 4-chloroaniline in fish would reach zero in 60 days. The doses over the 60-day period are then used to get the average lifetime realistic and worst case doses.

Accidents

To evaluate the risk of cancer from accidental exposures to the chemicals, it is necessary to determine the average lifetime doses from these exposures. (These are discussed in detail on pages F-84 through F-86 of Appendix F.) Dermal doses are multiplied by the dermal absorption rate (10 percent) and then divided by days in a lifetime to get the average lifetime dose from accidents. Oral doses are divided by days in a lifetime.

It should be noted that averaging a single large dose over a 70-year period creates uncertainty in the cancer risk calculations discussed in the risk evaluation section. That is, the actual risks of getting cancer could be higher or lower than those presented in this analysis.

A single large dose from an accident, which might occur only once in a lifetime, might overwhelm the body. That is, with such a high dose, the body's normal ability to get rid of the poison or repair damage it caused might fail. In that case, the risk of getting cancer from exposure to the chemical would be higher than the risk determined here.

On the other hand, the risk might be lower than that risk. For humans, the chemical would be in the body for only 1 day in a 70-year lifetime. To get the cancer potency, animals were given daily doses over a period about as long as the animal's natural lifetime.

Population at Risk

The number of people within the general public who could be exposed during gypsy moth operations is estimated to be 14 people per acre. (A detailed discussion of how this number was determined is on pages F-64 and F-65 in Appendix F.)

Forest Service records show that, on average, the insecticides have been used yearly on a total of about 385,000 acres. Assuming 14 people per acre, the number of people in the general public who potentially could be affected by gypsy moth control projects is about 5.4 million. Among these 5.4 million people, there are individuals or groups (for example, infants) who might be more sensitive than most people to the four insecticides. It is not possible to determine how many people would fall into the "sensitive category." But to be cautious, this group is included in the discussion regarding potential health effects.

RISK EVALUATION

What, then, are the risks to the health of workers and the general public from exposure to these insecticides?

These risks are determined by comparing the estimated exposure levels (from the exposure analysis and shown in Tables H-4 and H-5) with the toxic effect levels (from the hazard identification and shown in Table H-1). Such a comparison indicates whether harm will be caused if the exposure occurs. The odds of these exposures occurring is another question.

It is important to understand that some of the exposure scenarios are much less likely to occur than others. Because of the 10-percent correction for normal variations in mixing and spraying, even the realistic doses in the routine scenarios are higher than should occur in most sprayings. The worst case doses in the routine scenarios are far more unlikely. At most, there would be only 1 worst case exposure for every 500 realistic exposures.

A review of accidents in insecticide-spraying projects suggests that there would be 1 aircraft spill on land for about every 2,000 flights and 1 spill on water for about every 17,000 flights. Based on the yearly number of flights in the past, this suggests that gypsy moth projects could have about 2 aircraft spills every 3 years. Spills would involve worst case loads once every 800 years.

While truck accidents could lead to the highest exposures, these exposures are the least likely to occur. Based on national accident statistics for similar types of vehicles, trucks used in gypsy moth projects would have 1 accident for every 3 million miles traveled. Truck accidents involving spills would occur less than once every 8 million miles. Assuming that trucks carrying insecticides travel an average of 100 miles per project, truck spills on land

would occur once every 93,000 trips and on water once every 800,000 trips. The odds of a truck spill on land occurring in association with a worst case dose is about 1 in 50 million; on water, 1 in 460 million.

Threshold Responses

The comparisons for threshold responses for all four chemicals under all the exposure scenarios are listed in Table H-8. When the estimated dose might occur more than once, it is compared to the acceptable daily intake. High one-time doses from accidental spills are compared to the acute lethal dose for dermal exposure.

It must be emphasized that the comparisons with ADI's and LD_{50}'s could be misleading. The estimated doses from spraying mostly would be one-time or of short duration. Yet the ADI's are doses that can be safely taken every day for a lifetime. So it would seem reasonable that an estimated dose could exceed the ADI by a small amount without causing harm. With regard to the dermal LD_{50}'s, it is important to remember that, for all four chemicals, these were the highest doses tested and that they were not lethal. So a dose that exceeds the dermal LD_{50} might not be as harmful as it seems.

Except for most doses resulting from accidents, all realistic doses to the general public are the same as or below the ADI's. In most cases, workers also receive realistic doses that are below the ADI's. Mixer/loaders could receive realistic doses of acephate and trichlorfon that are slightly above the ADI's. For both the general public and workers, some routine exposures under the worst case lead to doses above the ADI's. All such exposures to the general public include eating food and drinking water containing spray residues. Every dose from routine operations is below the level that could cause birth defects and should be within the margin of safety for the general population in this regard. (To illustrate the concept of margin of safety, Figure H-7 compares the worst case dietary dose of trichlorfon with two of that chemical's NOEL's.)

Estimated doses that are the same as or below the ADI are considered safe and would pose no health risks. Estimated doses that are above the ADI or that are near or above the LD_{50} are another matter. In those cases it is necessary to take a closer look to determine the following:

- How close are the doses to the NOEL's? That is, what are the margins of safety?
- What might happen to the exposed person?
- What are the odds that the exposure would occur?

The following sections provide that closer look.

Table H-8.--Comparison of estimated doses to established safe doses and acute lethal doses for each insecticide under different exposure scenarios.

Exposure Scenario	Realistic Exposures: Relationship of Estimated Dose to: Acceptable Daily Intake (ADI)	Realistic Exposures: Relationship of Estimated Dose to: Acute Lethal Dose (Dermal LD_{50})	Worst Case Exposures: Relationship of Estimated Dose to: Acceptable Daily Intake (ADI)	Worst Case Exposures: Relationship of Estimated Dose to: Acute Lethal Dose (Dermal LD_{50})
		Acephate		
Routine Operations				
Workers				
Mixer/Loaders	Above		Above	
Observers	Below		Above	
General Public				
Direct	Below		Below	
Drift	Below		Below	
Indirect	Below		Below	
Direct plus dietary	Same		Above	
Indirect plus dietary	Same		Above	
Observer plus dietary	Same		Above	
Dietary only	Same		Above	
Accidents				
Aircraft spill				
Dermal (partial)		Below		Below
Dermal (full)		Below		Below
Water drinking	Same		Above	
Truck spill				
Dermal		Same		Above
Drinking water	Above		Above	
		Carbaryl		
Routine Operations				
Workers				
Mixer/Loaders	Below		Above	
Observers	Below		Below	
General Public				
Direct	Below		Below	
Drift	Below		Below	
Indirect	Below		Below	
Direct plus dietary	Below		Same	
Indirect plus dietary	Below		Same	
Observer plus dietary	Below		Above	
Dietary only	Below		Same	
Accidents				
Aircraft spill				
Dermal (partial)		Below		Below
Dermal (full)		Below		Below
Water Drinking	Same		Same	
Truck spill				
Dermal		Above		Above
Drinking water	Above		Above	

Table H-8.--Continued

Exposure Scenario	Realistic Exposures: Relationship of Estimated Dose to: Acceptable Daily Intake (ADI)	Realistic Exposures: Relationship of Estimated Dose to: Acute Lethal Dose (Dermal LD_{50})	Worst Case Exposures: Relationship of Estimated Dose to: Acceptable Daily Intake (ADI)	Worst Case Exposures: Relationship of Estimated Dose to: Acute Lethal Dose (Dermal LD_{50})
		Diflubenzuron		
Routine Operations				
Workers				
Mixer/Loaders	Below		Same	
Observers	Below		Below	
General Public				
Direct	Below		Below	
Drift	Below		Below	
Indirect	Below		Below	
Direct plus dietary	Below		Same	
Indirect plus dietary	Below		Same	
Observer plus dietary	Below		Same	
Dietary only	Below		Same	
Accidents				
Aircraft spill				
Dermal (partial)		Below		Below
Dermal (full)		Below		Below
Drinking water	Below		Below	
Truck spill				
Dermal		Below		Below
Drinking water	Same		Above	
		Trichlorfon		
Routine Operations				
Workers				
Mixer/Loaders	Above		Above	
Observers	Below		Above	
General Public				
Direct	Below		Same	
Drift	Below		Below	
Indirect	Below		Below	
Direct plus dietary	Same		Above	
Indirect plus dietary	Same		Above	
Observer plus dietary	Same		Above	
Dietary only	Same		Above	
Accidents				
Aircraft spill				
Dermal (partial)		Below		Below
Dermal (full)		Below		Below
Water Drinking	Above		Above	
Truck spill				
Dermal		Above		Above
Drinking water	Above		Above	

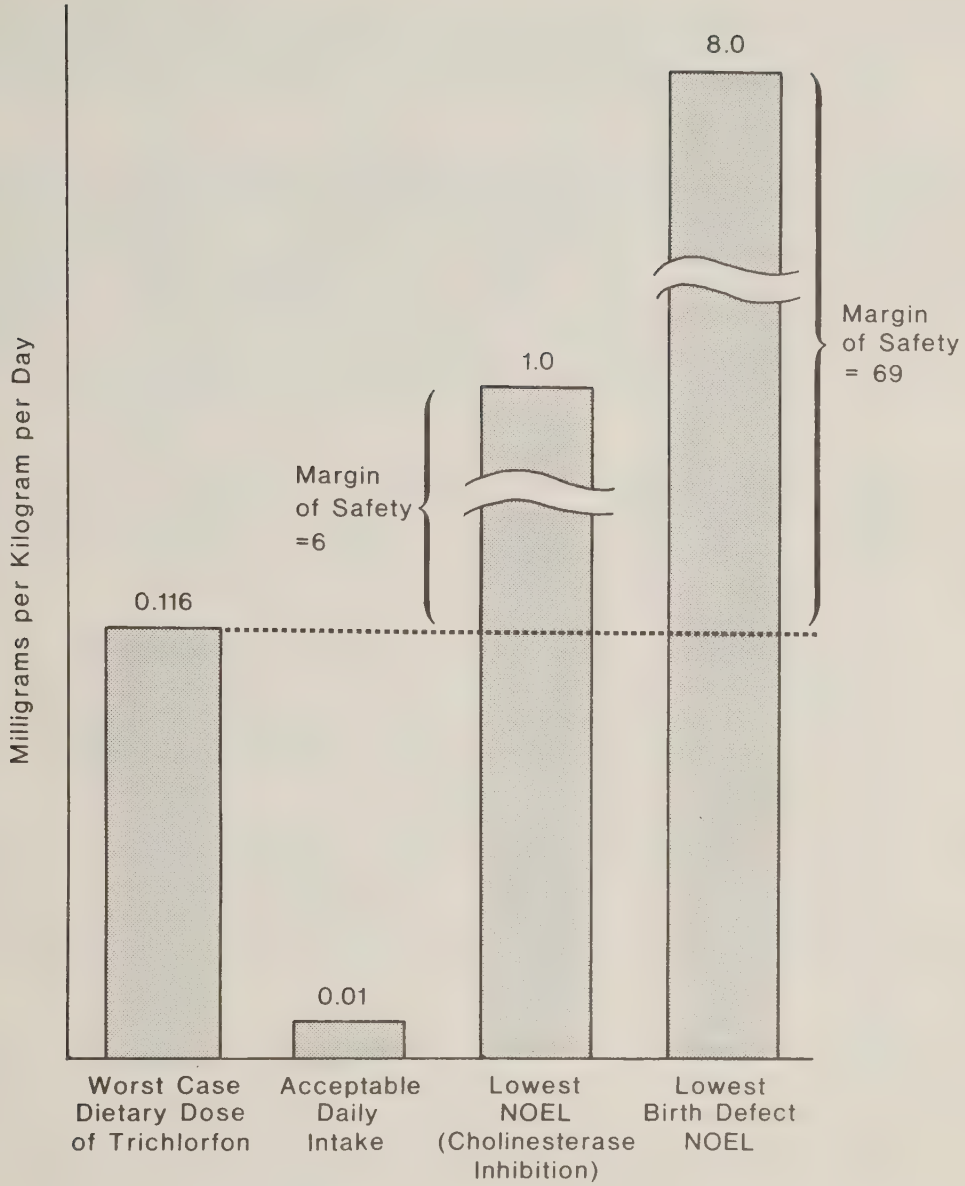

Figure H-7.--Illustration of how margins of safety are determined. This example compares the estimated worst case dietary dose of trichlorfon with two of that chemical's NOEL's. The estimated dose is 6 times below (one-sixth) the lowest NOEL and 69 times below the lowest birth defect NOEL.

Acephate

Routine Operations--Workers. The highest dose is the worst case dose to mixer/loaders. This dose is 6 times above the ADI and half the lowest NOEL, which is for cholinesterase inhibition. These workers thus might have temporary symptoms of cholinesterase inhibition. These symptoms

could include headaches, dizziness, blurred vision, or nausea. But it should be noted that a study of plant and lab workers exposed to acephate found no effects on blood cholinesterase levels.

Routine Operations--General Public. Worst case doses that include the dietary component are 4 to 6 times above the ADI. These worst case doses are half the lowest NOEL, so there might be some of the same symptoms of mild cholinesterase inhibition. Again, these effects would be temporary. The chance of birth defects is remote since the highest dose is about 70 times below the lowest birth defect NOEL.

Accidents. Dermal exposures from aircraft spills result in doses that range from 47 times to 177 times below the dermal LD_{50}. While there should be no deaths, the exposed persons could suffer from headaches, dizziness, nausea, abdominal cramps, diarrhea, or sweating.

Dermal exposures from a tank truck accident are up to twice as high as the dermal LD_{50}. It is not known for sure what the effects of such an exposure would be, though cholinesterase inhibition surely would occur. Possible symptoms include unconsciousness, breathing problems, convulsions, vomiting, harm to the nervous system, or even death if they do not get prompt treatment. This type of poisoning can be treated with atropine sulfate, a common antidote. While the truck spill poses the greatest health hazard, it has the lowest odds of occuring--about 1 in 100,000.

The worst case dose from drinking water contaminated by an aircraft spill is twice the ADI (one-fourth the NOEL). The realistic dose from drinking water with insecticide from a truck spill is 10 times above the ADI and the same as the lowest NOEL. The worst case drinking water dose from a truck spill is twice the NOEL. These three doses that exceed the ADI may well result in temporary signs of cholinesterase inhibition (such as headaches, dizziness, and nausea).

Carbaryl

Routine Operations--Workers. The worst case dose to mixer/loaders is twice the ADI, but 16 times below the lowest NOEL. The lowest NOEL is for birth defects in dogs. But there is doubt that this NOEL can be related to humans. As discussed in the hazard section, dogs seem uniquely sensitive to carbaryl. Birth defect NOEL's from tests using other mammals are much higher, and EPA has concluded that carbaryl will not cause birth defects in humans. Disregarding tests that used dogs, the lowest NOEL is for

cholinesterase inhibition, and the margin of safety with respect to it is 50. So it is unlikely that the mixer/loaders would have any ill effects.

Routine Operations--General Public. It is unlikely that there would be any ill effects to the general public from carbaryl spraying. The four worst case doses that include food and water with spray residues are equal to or slightly above the ADI. An observer who eats food and drinks water containing spray residues receives a dose 18 times below the lowest (dog) NOEL. For the lowest non-dog NOEL, the margin of safety is 57. So again it is unlikely that there would be any effects.

All realistic doses of carbaryl pose no threat of causing birth defects. But, assuming that carbaryl can cause birth defects in humans, the worst case doses might pose some risk of birth defects to sensitive individuals. These doses would be about 1,000 times below the lowest non-dog NOEL's for birth defects. This margin of safety, along with the low probability of a worst case exposure occurring (less than 1 chance in 500), suggests that the risk of birth defects even in sensitive individuals is quite low.

Accidents. All dermal exposures received from aircraft spills are far below the dermal LD_{50}. Realistic and worst case dermal exposures received from a truck spill are three times above the dermal LD_{50}. Without prompt medical help, such a dose could cause convulsions, shortness of breath, unconsciousness, or even death. Again, there is a common antidote that could reverse most symptoms. There is about 1 chance in 100,000 that such a spill would occur.

Drinking water containing insecticide from a truck spill results in a dose that is 6 times above the ADI. This dose is 5 times below the lowest NOEL and could result in cholinesterase inhibition. If the water were drunk for a week or two, there might be a chance of birth defects. There is a one in a million chance that such a spill would occur.

Diflubenzuron

Routine Operations--Workers. All doses are below or equal to the ADI.

Routine Operations--General Public. All doses are below or equal to the ADI. But there may be two groups that would be at greater risk than the public at large. They are people with genetic defects that make them prone to having methemoglobin in the blood, and very young infants who lack enzymes that can reduce the level of methemoglobin. To

avoid potential ill effects on these two groups, measures should be taken before spraying to alert them of the possible dangers.

Accidents. All dermal exposures result in doses that are below the dermal LD_{50}. All drinking water doses are below or equal to the ADI.

Trichlorfon

Routine Operations--Workers. Realistic doses to mixer/loaders are 5 times above the ADI. These doses are 22 times below the lowest NOEL, which is for cholinesterase inhibition. Worst case doses to observers are 6 times above the ADI (17 times below the lowest NOEL), and worst case doses to mixer/loaders are 20 times above the ADI (5 times below the NOEL). These workers thus run the risk of cholinesterase inhibition. Symptoms, which would be temporary, could range from eye irritation to headaches and nausea.

Routine Operations--General Public. The only doses that might be harmful to the general public are the worst case doses that include food and water containing spray residues. These doses range from 12 to 17 times above the ADI. The margin of safety with respect to the lowest NOEL ranges from 6 to 8. Symptoms might include eye irritation, dizziness, or headaches.

Worst case doses of trichlorfon pose some risk of birth defects to sensitive individuals. The highest dose (observer plus dietary) has a margin of safety of 46 with respect to the lowest birth defect NOEL. This is less than the safety factor of 100 used in determining the ADI. It is important to note that this NOEL (from a study using rats) is the highest dose tested and that this dose did not cause birth defects. The next highest birth defect NOEL is from a study that used hamsters and is 25 times higher. If that NOEL were used, the margin of safety would be more than 1,000. Given the low odds for a worst case exposure, the risk of birth defects even in sensitive individuals is quite low.

Accidents. Truck accidents could be quite hazardous. Dermal exposures from truck accidents are 5 times the dermal LD_{50}. The poisoning could affect the lungs and the nervous system, and it could cause convulsions, unconsciousness, or even death. Again, there is a common antidote, so most symptoms could be reversed with prompt medical help.

The doses received from drinking water containing trichlorfon residues from accidental aircraft spills range from 3 to 6 times above the ADI (30 to 17 times below the lowest NOEL). Doses from drinking water following a truck spill are 23 times above the ADI (one-fourth the NOEL) for both the realistic and worst cases. These drinking water doses could lead to mild symptoms of cholinesterase inhibition. These temporary symptoms could include eye irritation, dizziness, headaches, or nausea.

Nonthreshold Reponses

Cancer

It was assumed that using any of the four chemicals might lead to cancer. The probability of cancer being caused by exposure to a chemical is determined by multiplying its cancer potency for humans (as derived through use of the linear model) by the lifetime average daily dose under each of the exposure scenarios.

The cancer probabilities are listed in Table H-9. The numbers in this table are weighted lifetime risks for all people who are exposed. They assume a person is exposed to the chemical, but they also take into account the odds of

Table H-9.--Weighted risk of cancer to individual if exposed to insecticide under different exposure scenarios. (chances in a million over a lifetime)

Exposure Scenario	Acephate	Carbaryl[a]	Diflubenzuron[b]	Trichlorfon
Routine Operations				
Eradication projects	1.4	0.0021	0.0012	0.08
Suppression projects	2.4	0.0035	0.0023	0.13
Cumulative eradication and suppression projects	3.8	0.0055	0.0035	0.21
Accidents				
Aircraft Spill				
Dermal (partial)	5.7			1.1
Dermal (full)	12			2.2
Drinking water	0.032	0.0004		0.0068
Eating fish			0.0001	
Truck spill				
Dermal		1,000		190
Drinking water	.24	0.0031		0.042
Eating fish			0.00067	

[a]Statistic is for risk of cancer from N-nitrosocarbaryl. If the higher cancer potency discussed on page H-13 were used, all the cancer risks would still be less than 1 in a million.

[b]Statistic is for risk of cancer from 4-chloroaniline.

realistic and worst case exposures occurring. (At most, there would be 1 worst case dose for every 500 realistic doses.) A worst case dose could raise the odds of cancer two- to twelve-fold. The meaning of the numbers in Table H-9 can be lost without reference to other commonly known health risks. For example, the riskiest of the routine scenarios in terms of cancer clearly is the one in which acephate is used to both eradicate and suppress gypsy moths. Under that scenario, the odds of getting cancer from acephate are less than 4 in a million. A person would have the same chance of getting cancer by smoking about 8 cigarettes in his or her lifetime.

To evaluate fully the risk of cancer from an accident, the chances of the accident occurring also should be considered. For example, the odds are about 2 in a million that an individual completely doused with trichlorfon from an airplane spill would get cancer. At the same time, such a spill only would occur in about 1 out of every 2,000 trips, and even then it would be highly unlikely for a person to be doused. Thus, when the cancer risks related to accidents are considered along with the low probability of an accident occurring, the chances of cancer resulting from an accident become remote.

Acephate. The cancer risk was calculated for persons who receive a direct application and who eat and drink food and water with spray residues. These are the people in the general public who receive the highest exposures.

The weighted lifetime cancer risk from exposure to acephate is 1.4 in a million for eradication projects, 2.4 in a million for suppression projects, and 3.8 in a million for the combination of both. There would be less than one incidence of cancer for every 300,000 acres sprayed. In the past, acephate has been used on less than 1,000 acres per year. Thus the added risk of cancer from using acephate could be about 0.003 incidences per year in the exposed population of 14,000 people.

Carbaryl. For carbaryl, the only doses relevant to cancer are those obtained through eating and drinking. This is because N-nitrosocarbaryl could be formed only through ingestion of carbaryl.

The weighted cancer risk for carbaryl (from the formation of N-nitrosocarbaryl) is 2.1 in a billion for eradication projects, 3.5 in a billion for suppression projects, and about 5.5 in a billion for the combination of both. (If the higher cancer potency discussed on page H-13 were used, the cancer risks would still be less than 1 in a million.) There would be less than one incidence of cancer for every 150 million acres sprayed. In the past, carbaryl has been

used on about 82,000 acres per year. Thus the added risk of cancer from using carbaryl could be about 0.0004 incidences per year in the exposed population of 1.14 million people.

Diflubenzuron. The potential cancer risk from diflubenzuron comes from eating meat or fish containing 4-chloroaniline, a breakdown product of diflubenzuron. The data in Table H-9 assume that a person eats meat or fish exposed to diflubenzuron.

The weighted cancer risk from eating fish or meat containing 4-chloroaniline (from the breakdown of diflubenzuron) is about 1.2 in a billion for eradication projects, 2.3 in a billion for suppression projects, and 3.5 in a billion for the combination of both. There would be less than one incidence of cancer for every 300 million acres sprayed. In the past, diflubenzuron has been applied to about 141,000 acres per year. Thus the added risk of cancer from using diflubenzuron could be about 0.0005 incidences per year in the exposed population of 2 million people.

Trichlorfon. The cancer risk from exposure to trichlorfon was calculated for members of the general public with the highest exposure. These are persons who receive a direct application and who then eat and drink food and water containing spray residues. Those with lower exposures will have correspondingly lower cancer risks.

The weighted cancer risk from exposure to trichlorfon in eradication projects is less than 1 in 10 million. The weighted lifetime cancer risk for exposure from suppression projects is about 1 in 7 million, with the weighted lifetime risk from combined projects being about 2 in 10 million. There would be less than one incidence of cancer for every 5 million acres sprayed. Each year, approximately 161,000 acres have been sprayed with trichlorfon. Thus the added risk of cancer from using trichlorfon could be about 0.03 incidences in the exposed population of 2.25 million people.

Heritable Mutations

The risk of heritable mutations is based on the overall evidence of whether or not the insecticides are mutagenic in humans. As indicated in the hazard identification, diflubenzuron is considered to be non-mutagenic; acephate probably cannot cause mutations in whole mammals; carbaryl is only weakly mutagenic; while trichlorfon appears to be a mutagen that can reach germ cells. At the worst case, the probability of acephate, carbaryl, or trichlorfon causing mutations would be no greater than the probability of it causing cancer.

Synergistic and Cumulative Effects

Because of chemicals already in the environment, it is possible that the risks from using these four insecticides might be greater than described.

First, any of the four insecticides might combine with different chemicals in the environment. By doing so, they might create effects that are greater than the sum of their separate effects. This process is called synergism. Since there are many possible combinations that could occur, it is hard to predict the effects of synergism. But based on studies of carbaryl and other chemicals, a 10-fold increase in toxic levels in isolated instances seems to be the most that could happen. This would be the worst case. Most margins of safety would still be acceptable for the general public, but sensitive individuals could be at risk.

Second, any of the four chemicals might be in the environment from other sources. So gypsy moth spraying could add to the amounts that are already there. Especially in the case of carbaryl or acephate, homeowners might be using these chemicals in their gardens. Other sources might be food and drift from farm areas where these chemicals are used. But data on chemical residues in food suggest that there would be little, if any, cumulative effect from these four insecticides. (For more details about synergistic and cumulative effects, see pages F-101 to F-104 in Appendix F.)

Preparers

This plain language summary of the health risk analysis was prepared under contract by Labat-Anderson Incorporated. The principal preparers were the following:

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Appendix I
Clarification of Information About the Toxicity of Acephate, Carbaryl, Diflubenzuron, and Trichlorfon

INTRODUCTION

This appendix corrects, clarifies, or explains information in the 1985 Final Environmental Impact Statement, including Appendix F. Most of this information was presented in court during Oregon Environmental Council v. Kunzman.

REVIEW OF TOXICITY STUDIES

This section describes more completely the toxicity information that was summarized in Tables 1 through 7 in Appendix F. This information is being included to clarify for the reader the potential hazards of the insecticides. In addition, this information clarifies the background and basis for selecting the no-observed-effect levels (NOEL's) used in the worst case analysis. This section also provides the descriptive background needed to identify possible health effects resulting from exposure to insecticides used to control the gypsy moth.

Results of Studies

Acephate

Acute Toxicity Studies. Based on an acute oral LD_{50} (median lethal dose) in rats ranging from 866 mg/kg (females) to 945 mg/kg (males), acephate can be classified as a moderately toxic insecticide (U.S. EPA, 1984a). An acute delayed neurotoxicity study did not produce leg paralysis in rats exposed to 375 mg/kg/day, which was the highest dose tested (U.S. EPA, 1982). The acute dermal LD_{50} for rabbits was reported to be greater than 10,000 mg/kg (U.S. EPA, 1984a).

Subchronic Studies. The predominant toxic effect seen in test subjects after exposure to acephate is a decreased level of red blood cell, plasma, and brain cholinesterase. An *in vitro* cholinesterase inhibition assay using rat, monkey, and human cells resulted in poor inhibition of acetyl cholinesterase and cholinesterase activities in all test species (U.S. EPA, 1984a). A 21-day rat feeding study resulted in a no-observed-effect level (NOEL) less than 30 ppm (1.5 mg/kg/day); 30 ppm was the lowest dose tested and resulted in a 21-percent inhibition of red blood cell cholinesterase during the second test week and a 15-percent inhibition during the third test week (U.S. EPA, 1984a). A 21-day dermal rabbit study resulted in 51 to 54 percent inhibition of red blood cell cholinesterase at the dose levels of 0.5, 1.0, and 2.0 g/kg (U.S. EPA, 1984a). A 33- to 34-day oral cholinesterase study during which monkeys

were exposed to acephate resulted in a 50-percent reduction of plasma, red blood cell, and brain cholinesterase levels, and a 5- to 17-percent reduction in the level of cerebrospinal cholinesterase (U.S. EPA, 1984a). A 90-day rat cholinesterase study established a NOEL of 5 ppm (0.25 mg/kg) for brain, red blood cell, and plasma cholinesterase levels (U.S. EPA, 1984a).

Chronic and Oncongenic Studies. A 2-year validated Industrial Bio-Test dog feeding study established a systemic NOEL greater than 100 ppm (2.5 mg/kg/day) based on the absence of toxic systemic effects; however, a cholinesterase NOEL of 30 ppm (0.75 mg/kg/day) was reported with reduced levels of red blood cell, plasma, and brain cholinesterase observed at 100 ppm (2.5 mg/kg/day) (U.S. EPA, 1984a).

A 28-month oncogenic rat feeding study resulted in the establishment of a NOEL at 5 ppm (0.25 mg/kg/day) based on inhibition of plasma, red blood cell, and brain cholinesterase levels at the higher doses tested. Histopathological examination of tissue specimens revealed no evidence of carcinogenic effects at the highest dose level of 700 ppm (105 mg/kg/day) (U.S. EPA, 1982).

A 2-year oncogenic study during which mice were exposed to 1,000 ppm (150 mg/kg/day) of acephate resulted in a 15.8 percent incidence of liver tumors and a 19.7 percent incidence of excessive noncancerous cell growth in females. Liver and lung injuries were observed at all testing levels. At the dose level of 1,000 ppm (150 mg/kg/day), weight alteration was observed in the livers, kidneys, brain, and ovaries. Decreased body weight gain was also observed in test animals at 1,000 ppm (150 mg/kg/day) (U.S. EPA, 1984a).

Teratology Studies. Teratogenic effects have not been induced in laboratory animals upon maternal exposure to acephate during gestation. A validated Industrial Bio-Test rat teratology study reported a teratogenic NOEL greater than 200 mg/kg (highest dose tested) (U.S. EPA, 1984a; U.S. EPA, 1982). A rabbit teratology study also resulted in a teratogenic NOEL greater than the highest dose level of 10 mg/kg; however, a maternal toxic NOEL of 3 mg/kg was reported based on increased nasal discharge and increased incidence of abortions (U.S. EPA, 1984a).

Mutagenicity Studies. Acephate has been shown to be weakly mutagenic in studies with bacteria, fungi, and mammalian cells in culture. However, a number of *in vivo* tests have been negative, including mouse dominant lethal, mouse bone marrow cytogenetic, monkey and mouse sister chromatid exchange, and *Drosophila* sex-linked recessive assays (U.S. EPA, 1984a).

Carbaryl

A summary of established no-observed-effect levels (NOEL's) for carbaryl for various mammals is shown in Table I-1. This table clarifies Table 2 of Appendix F (pages F-115 and F-116).

Acute and Subchronic Studies. Based on the acute oral LD_{50} for rats of 270 mg/kg, carbaryl can be classified as a moderately toxic insecticide (U.S. EPA, 1984b). The acute oral LD_{50} for dogs was reported to be less than 500 mg/kg, and the acute oral LD_{50} for monkeys was established as greater than 1,000 mg/kg (U.S. EPA, 1984b). The acute dermal LD_{50} for rats was reported to be greater than 4,000 mg/kg and the acute dermal LD_{50} for rabbits was reported to be greater than 5,000 mg/kg (U.S. EPA, 1984b).

Acute and subchronic exposure to carbaryl by human subjects has been documented in poisoning incidents, worker exposure studies, and volunteer ingestion studies. Ingestion of 2.8 mg/kg of carbaryl (Sevin formulation) resulted in epigastric pain and sweating. Toxic effects were relieved by the administration of the antidote atropine sulfate (Harry, 1977). Ingestion of carbaryl at the dose levels of 0.25, 0.5, 1.0, and 2.0 mg/kg by 10 volunteer subjects resulted in nausea and vomiting in one test subject at the highest dose tested (2.0 mg/kg). No toxic effects were observed at the other doses tested (Harry, 1977). Subacute dermal and inhalation exposure of carbaryl production workers at 0.44 to 4.9 mg/m^3 did not produce abnormal sperm count or infertility after a 1-year exposure period (U.S. EPA, 1984b).

Subchronic and acute exposure to carbaryl has resulted in decreased levels of cholinesterase and decreased reabsorption by proximal tubules of the kidney in test animals and humans. Cholinesterase is instrumental for the normal propagation of a nerve impulse because of its role in bond cleavage of the neural transmitter acetyl choline. Both these toxic effects are transitory and have not resulted in permanent physiological damage to the exposed individuals (Harry, 1977, and Wills et al., 1968).

An acute oral cholinesterase LD_{50} rat study reported significant depression of plasma, red blood cell, and brain cholinesterase in the surviving test animals. A second acute oral cholinesterase study resulted in depression of the red blood cell cholinesterase level in rats after exposure to carbaryl (in propylene glycol) at the dose of 12.5 mg/kg after 1 and 4 hours (U.S. EPA, 1984b). A 7-day rat cholinesterase study reported a NOEL of 10 mg/kg, with

Table I-1.--Summary of established no-observed-effect levels (NOEL's) for carbaryl for various mammals.

Test Animal	Type of Test	Results	Reference
		General Toxicity	
Rat	2-year feeding	Systemic NOEL = 200 ppm LOAEL = 400 ppm (swelling of kidneys and liver)	Carpenter et al., 1961
	7-day feeding	ChE NOEL = 10 mg/kg/day LOAEL = 50 mg/kg/day (53% decrease in ChE)	U.S. EPA, 1984b
Dog	1-year feeding	ChE NOEL > 7.2 mg/kg/day	Carpenter, 1961
		Systemic NOEL = 1.8 mg/kg/day LOAEL = 7.2 mg/kg/day (swelling in kidney)	Carpenter, 1961
Human	Subacute	NOEL = 0.06 mg/kg/day LOAEL = 0.13 mg/kg/day (reversible decrease of reabsorption of amino acids by proximal tubules)	U.S. EPA, 1984b
Pig	Neurotoxicity	LOAEL = 150 mg/kg/day	Smalley et al., 1969

Table I-1 (continued).--Summary of established no-observed-effect levels (NOEL's) for carbaryl for various mammals.

		Teratogenic/reproductive	
Mouse	Teratogenic (diet)	Teratogenic NOEL > 1,166 mg/kg/day Maternal LOAEL = 1,166 mg/kg/day (decreased weight gain) Fetotoxic LOAEL = 1,166 mg/kg/day (reduced embryo weight)	Murray et al., 1979
	(gavage)	Teratogenic NOEL > 150 mg/kg/day Maternal LOAEL = 150 mg/kg/day (decreased weight gain, ChE inhibition)	Murray et al., 1979
Rabbit	Teratogenic (gavage)	Teratogenic NOEL = 150 mg/kg/day Teratogenic LOAEL = 200 mg/kg/day (omphalocele) Maternal NOEL = 150 mg/kg/day (weight loss)	Murray et al., 1979
	Teratogenic (diet/capsule)	Teratogenic NOEL > 200 mg/kg/day	Robens et al., 1969
Rat	Teratogenic (diet)	Teratogenic NOEL > 500 mg/kg/day Maternal LOAEL = 500 mg/kg/day (decreased weight gain) Fetotoxic LOAEL = 500 mg/kg/day	Weil et al., 1972
	Reproductive (3 generation) (diet)	Reproductive NOEL > 10 mg/kg/day Maternal LOAEL = 10 mg/kg/day Fetoxicity LOAEL = 10 mg/kg/day (dilated uterine gland in third generation pups)	Weil et al., 1972
	Reproductive (3 generation) (diet)	Reproductive NOEL = 200 mg/kg/day	Weil et al., 1973

Table I-1 (continued).--Summary of established no-observed-effect levels (NOEL's) for carbaryl for various mammals.

	gavage	Reproductive NOEL = 25 mg/kg/day Maternal LOAEL = 100 mg/kg/day (decreased weight gain, ChE inhibition) Fetotoxic LOAEL = 100 mg/kg/day (decreased number of fetus)	Weil et al., 1973
Guinea Pig	Teratogenic (diet)	Teratogenic NOEL > 300 (HDT) Maternal NOEL > 300 Fetotoxic NOEL > 300	Weil et al., 1973
		Teratogenic NOEL < 300	Robens et al, 1969
	Teratogenic (gavage)	Teratogenic NOEL > 200 (HDT) Maternal LOAEL = 200 mg/kg/day (decreased weight gain) Fetotoxic NOEL > 200 mg/kg/day (HDT)	Weil et al., 1973
Dog	Teratogenic (diet)	Teratogenic NOEL = 3.125 Teratogenic LOAEL = 6.25 (lack of tail, abdominal fissure, failure of skeletal formation and extra toes)	Smalley et al., 1978
		Mutagenicity	
Mouse	Dominant lethal	NOEL > 200 mg/kg/day	Epstein et al., 1972

decreased levels of red blood cell cholinesterase observed at the lowest-observed-adverse-effect level (LOAEL) of 50 mg/kg (U.S. EPA, 1984b). Dermal application of carbaryl (5 percent Sevin 85W) to 10 human test subjects resulted in depressed red blood cell cholinesterase levels after 24 hours; however, 5 days after exposure, the cholinesterase levels were within normal levels (Harry, 1977).

A 6-week subacute human ingestion study during which doses of 0.06 mg/kg and 0.13 mg/kg were administered daily resulted in no toxic effects at the dose level of 0.06 mg/kg. A reversible decrease in the reabsorption capacity in the proximal tubule of the kidney was observed in test subjects after the 6-week exposure to 0.13 mg/kg of carbaryl (Wills et al., 1968).

Chronic Studies. A 1-year dog feeding study resulted in toxic effects reported as morphological changes in the kidneys of test animals but no apparent decrease in the level of cholinesterase. The cholinesterase NOEL was reported to be greater than 7.2 mg/kg (highest dose tested) (U.S. EPA, 1984b). A systemic NOEL of 1.8 mg/kg and a LOAEL of 7.2 mg/kg were reported based on diffuse cloudy swelling or vacuolization of kidney cells (U.S. EPA, 1984b). Similar histological effects have been observed in the kidneys of rats and monkeys after exposure to carbaryl (Wills et al., 1968).

A 2-year rat feeding study reported a systemic NOEL of 200 ppm (10 mg/kg/day). At the highest dose level of 400 ppm (20 mg/kg/day), morphological changes characterized by cloudy swelling were observed within tubules of the kidney and hepatic cords of the liver (U.S. EPA, 1984b).

Teratogenic and Reproductive Studies. A study was conducted to evaluate the teratogenic potential of carbaryl when administered by gavage or in the diet to mice and rabbits during days 6 through 15 of gestation. Dietary administration to mice did not result in teratogenic effects. A teratogenic NOEL for mice greater than 1,166 mg/kg/day (only dose tested) was reported for dietary exposure, and a teratogenic NOEL greater than 150 mg/kg/day (highest dose tested) was reported upon administration of carbaryl by gavage. Fetotoxic effects in mice characterized by decreased maternal weight gain and reduced embryo development were observed at the dietary level of 1,166 mg/kg/day. A maternal NOEL less than 1,166 mg/kg/day was reported based on decreased weight gain. In the gavage study, decreased weight gain and cholinesterase inhibition were reported as maternal toxic effects. Administration of carbaryl by gavage to rabbits resulted in the establishment of a teratogenic NOEL of 150 mg/kg/day based on the occurrence of omphalocele (hernia of the naval). A dose of

200 mg/kg was reported as a maternal toxic dose, and 150 mg/kg was reported as a mild maternal toxic dose when administered by gavage to rabbits (Murray et al., 1979).

A teratology study using guinea pigs, rabbits, and hamsters resulted in teratogenic effects in guinea pigs, but no apparent malformations in hamsters and rabbits. Exposure of hamsters to carbaryl at levels of 125 to 250 mg/kg and rabbits at 50 to 200 mg/kg did not result in teratogenic effects. Teratogenic bone defects were observed in guinea pigs at the dose level of 300 mg/kg (Robens, 1969). However, another teratology study that exposed guinea pigs to 300 mg/kg/day of carbaryl did not produce teratogenic effects (Weil et al., 1973).

A teratology study that exposed rats to dietary doses up to 500 mg/kg/day of carbaryl did not result in teratogenic effects. Decreased weight gain was reported as a fetal toxic and maternal toxic effect at 500 mg/kg/day (Weil et al., 1972).

A three-generation reproduction study during which rats were exposed daily to carbaryl at 10 mg/kg did not significantly affect fertility, gestation, lactation, or viability of pups (Weil et al., 1972).

A second three-generation rat reproduction study established a reproductive NOEL of 200 mg/kg (highest dose tested) when carbaryl was administered as part of the diet (Weil et al., 1973).

A teratology study during which beagle dogs were exposed to 50, 25, 12.5, 6.25, and 3.125 mg/kg of carbaryl throughout the gestation period resulted in a teratogenic NOEL of 3.125 mg/kg. Defects included abdominal fissures, failure of skeletal formation, absence of tail formation, and the presence of extra toes (Smalley et al., 1968).

Mutagenicity Studies. A dominant lethal rat mutation assay was nonmutagenic upon exposure to 200 mg/kg of carbaryl (highest dose tested) (Epstein et al., 1972). However, chromosomal assays resulted in the induction of mitotic effects and chromosomal abberations (U.S. EPA, 1984b). The reproductive effects assessment group of the Environmental Protection Agency has concluded that data from mutagenic studies indicate that carbaryl does not act as a potent mutagen and can be classified as a weak mutagen (U.S. EPA, 1984b).

Oncogenic Studies. Despite speculation that carbaryl could combine with nitrite compounds to form a carcinogen under acidic conditions similar to those found in the human stomach, the majority of studies examining the carcinogenic

potential of carbaryl have been negative. A preliminary report by the carcinogen assessment group concluded that among treated animals there was no significant increase in the incidence of tumor induction relative to control animals (U.S. EPA, 1984b).

A 2-year oncogenic rat feeding study was negative for carcinogenic effects at 400 ppm (20 mg/kg/day), which was the highest dose tested (U.S. EPA, 1984b). An oncogenic mouse study during which carbaryl was either given orally at 464 mg/kg for 5 weeks, fed at the dose level of 14 ppm (2.1 mg/kg/day), or administered under the skin in a single dose of 100 mg/kg did not induce cancer in test animals (U.S. EPA, 1984b). Another oncogenic 2-year mouse study was negative at the dietary level of 400 ppm (60 mg/kg/day) (U.S. EPA, 1984b). An intraperitoneal oncogenic study during which mice were administered carbaryl at a dose level of 60 mg/kg/week did not induce oncogenic effects in test animals (U.S. EPA, 1984b). The injection under the skin of 5 percent (10 mg) of carbaryl for a 20-week test period was negative for oncogenic effects (U.S. EPA, 1984b). The dermal application of a 57-percent water dilution of carbaryl did not result in oncogenic effects (U.S. EPA, 1984b).

A 22-month rat feeding study at the dose level of 30 mg/kg (highest dose tested) resulted in the induction of malignant tumors in 4 out of 12 surviving test animals (U.S. EPA, 1984b). Oncogenic effects also were observed after the subcutaneous administration of 20 mg of carbaryl to 48 rats. Tumor formation was observed in 2 out of 10 surviving test animals. However, no significant increase in tumor incidence in treated groups relative to controls was found by the carcinogen assessment group of the Environmental Protection Agency (U.S. EPA, 1984b).

Viral Enhancement. The subject of viral enhancement was discussed on pages 59 and 60 of the Final Environmental Impact Statement. The following information was presented in court (Oregon Environmental Council v. Kunzman) and updates the discussion in the FEIS.

The interactions between viruses and chemical pesticides have been studied out of a concern that these interactions may affect human health. This is of concern because of the suggested link between certain viral diseases and Reye's syndrome. The Maine Bureau of Forestry appointed a health advisory panel to review the data available on Sevin-4-oil specific to viral potentiation; and, in January 1980, the panel released its findings and recommendations (see Appendix B of USDA, 1981). The panel found that "there was a potential but inconclusive health risk of Sevin-4-oil, on the basis of viral potentiation data available, and

recommended that the Maine Bureau of Forestry develop more stringent limitations so that "no uninformed, unconsented human exposure occurs during a forest spray operation." Abrahamsen and Jerkofsky (1981) described the enhancing effect of Sevin-4-oil on the replication of varicella-zoster virus (VZV) in cell culture, and suggested possible implications of this interaction with regard to Reye's syndrome. Since this study, others have been conducted that raise questions and uncertainty about the Abrahamsen and Jerkofsky study.

Schmidt (1983) found that carbaryl treatment of host cell cultures serves to delay the early spread of simian varicella viral infections. Schmidt suggested that the apparent effect seen by Abrahamsen and Jerkofsky occurred at a point in the growth cycle at which infectivity had reached maximum levels and was declining in untreated cultures, whereas the cells in the treated cultures, spared from early infection, had finally become infected. Schmidt also suggested that the proposed VZV-enhancing effect of carbaryl and the possible implications to Reye's syndrome might be reevaluated. In a recent study by Brookman et al. (1984), various insecticides, solvents, emulsifiers, and mixtures thereof were evaluated to determine whether any were capable of enhancing the sensitivity of cultured mammalian cells to infection with vesicular stomatitis virus. The investigation was replicated in three independent laboratories. None of the compounds, including the insecticide Sevin, significantly enhanced the viral infection.

N-nitrosocarbaryl Formation. The subject of N-nitrosocarbaryl formation was discussed on pages 60 and 61 of the Final Environmental Impact Statement. The following information was presented in court (Oregon Environmental Council v. Kunzman) and updates the discussion in the FEIS.

Under acidic conditions similar to those found in the human stomach, carbaryl has been nitrosated in the laboratory to the reaction product N-nitrosocarbaryl (Eisenbrand et al., 1975). Elespuru et al. (1974) found that the combination of sodium nitrite (a food additive) with carbaryl in acid solution results in the formation of nitrosocarbaryl. It is thought that human exposure to nitrosocarbaryl could occur from the reaction of carbaryl residues (in food) and sodium nitrite (in saliva or food) in the acid conditions of the stomach. N-nitrosocarbaryl has been characterized as a mutagen and a carcinogen based on positive laboratory studies (Eisenbrand et al., 1976, and Elespuru and Lijinsky, 1973). An oncogenic rat study resulted in the induction of malignant tumors at the injection site in 14 of 16 test animals after exposure to a dose level of N-nitrosocarbaryl at 1,000 mg/kg (Eisenbrand et al.,

1975). Rats that were administered N-nitrosocarbaryl by gavage developed a high incidence of stomach tumors (invasive squamous carcinomas) (Lijinsky and Taylor, 1976). A rat feeding study also resulted in the formation of stomach tumors (Lijinsky and Schmahl, 1978). N-nitrosocarbaryl appears to be a much less effective inducer of mouse skin tumors than other methylating agents such as nitrosomethylurea. Dermal application of N-nitrosocarbaryl (25 microliters of a 0.04 M solution) to the shaved skin of 20 mice led to the induction of skin tumors at the site of application in 8 of the test animals, but only after repeated dermal applications (twice a week for 50 weeks) to shaved skin. The skin tumors appeared in 1 of 20 animals at week 60, and in 8 of 20 by week 90 (Lijinsky and Winter, 1981). This indicates that N-nitrosocarbaryl could cause cancer in the stomach or on the skin if it could form in the environment as a result of carbaryl applications. However, the literature shows that N-nitrosocarbaryl only can form under conditions similar to those found in the human stomach--not in the air or on skin surfaces.

A bacterial assay study characterized nitrosocarbaryl as a potent mutagen because of the positive mutagenic response of carbaryl in two bacterial systems (Escherichia coli and Haemophilus influenzae) (Elespuru et al., 1974).

Diflubenzuron

Acute Toxicity Studies. Based on acute oral LD_{50} values greater than 4,640 mg/kg in rats and mice, diflubenzuron can be classified as a slightly toxic insecticide (U.S. EPA, 1984c). The acute dermal LD_{50} for rats was reported to be greater than 10,000 mg/kg, and for rabbits it was greater than 4,640 mg/kg (U.S. EPA, 1984c).

Chronic Toxicity Studies. The major toxic effect observed in test subjects upon exposure to diflubenzuron is the formation of sulfhemoglobin and methemoglobin pigments in the circulatory system. Hemoglobin in its nonoxidized state is essential for the transport of oxygen, whereas the oxidized form, methemoglobin, plays no role in oxygen transport. Investigators have suggested that there is a correlation between increased levels of methemoglobin and increased levels of sulfhemoglobin.

An 80-week mouse feeding study established a NOEL of 1.1 mg/kg/day based on the formation of methemoglobin and sulfhemoglobin in the test animals (U.S. EPA, 1984c). A 104-week rat feeding study resulted in a NOEL of 40 ppm (2 mg/kg/day) with increased levels of methemoglobin and sulfhemoglobin observed in test animals (EPA, 1984c). A lifetime oncogenic mouse feeding study also established a

NOEL of 16 ppm (2.4 mg/kg/day) based on increased levels of methemoglobin and sulfhemoglobin (U.S. EPA, 1984c).

Teratology and Reproductive Studies. Teratology studies in rats and mice did not result in teratogenic effects at the levels tested (U.S. EPA, 1984c). Maternal toxicity, fetal toxicity, and teratogenic NOEL's were established as being greater than 4,000 mg/kg (highest dose tested) for both test species (U.S. EPA, 1984c). A three-generation rat reproduction study resulted in the absence of reproductive toxic effects at 10, 20, 40, and 160 ppm (0.5, 1, 2, and 8 mg/kg/day) (U.S. EPA, 1984c; Uniroyal, 1983).

Mutagenicity Studies. Diflubenzuron was found to be nonmutagenic even at high dose levels (Quarles et al., 1980; MacGregor et al., 1979; and U.S. EPA, 1984c). Diflubenzuron did not produce a mutagenic response in hamster fetal cells at the concentration of 500 mg/kg body weight (Quarles et al., 1980). Negative results also were obtained for diflubenzuron in the mouse micronucleus test in vivo, the mouse lymphoma mutation assay, and the bacterial Ames mutation assay (MacGregor et al., 1979).

Oncogenic Studies. Evidence of oncogenicity was not observed in any test animals at doses as high as 1,000 ppm (150 mg/kg/day) in the lifetime oncogenic mouse study (U.S. EPA, 1984c). A second oncogenic study that used rats as the test species also resulted in the absence of oncogenic effects even at 10,000 ppm (500 mg/kg/day) (highest dose tested) (U.S. EPA, 1984c). Although diflubenzuron has not been shown to be carcinogenic, one of its metabolic breakdown products, 4-chloroaniline, has been claimed to be a carcinogen. This possibility is discussed in this appendix in the section on cancer potencies.

Possible Dioxin Contamination. The concern that diflubenzuron may possibly be contaminated with "dioxin" became an issue when a list of 60 pesticides possibly contaminated with dioxin was published in the February 20, 1985, issue of Pesticides & Toxic Chemical News. The list, which was contained in an internal memo prepared by EPA, included diflubenzuron. After discussion with EPA, USDA was able to determine that the list of possible pesticides contained any pesticide that contained a chlorine on benzene ring. EPA also informed USDA that they did not expect any 2,3,7,8-tetrachlorodibenzo-p-dioxin (the one, of 75 possible dioxin compounds, that people refer to as "dioxin") (U.S. EPA, 1985b). Duphar B.V., the registrant of diflubenzuron, has also tested for the possible presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin or tetrachlorodibenzofurans in technical grade diflubenzuron. They found no contamination using a testing method that had a sensitivity of 0.01 ppm (Shadbolt, 1985). From these

discussions, USDA concluded that there was no evidence to indicate that diflubenzuron is contaminated with "dioxin."

Trichlorfon

Acute Toxicity Studies. The lowest reported acute oral LD_{50} value for rats is 144 mg/kg (Mobay, 1981). However, based on the most commonly reported LD_{50} values ranging from 400 to 650 mg/kg, trichlorfon can be classified as a moderately toxic insecticide (International Agency for Research on Cancer (IARC), 1983). The acute dermal LD_{50} for rats was reported to be greater than 2,000 mg/kg (Mobay, 1981). The acute rat inhalation LC_{50} was reported to be greater than 10,000 mg/kg (Mobay, 1981).

Subchronic and Chronic Toxicity Studies. Feeding studies that lasted 3 months to 2 years resulted in cholinesterase inhibition at the dose level of 1.25 mg/kg/day in dogs and 2.5 mg/kg/day in rats (Doull et al., 1980). A NOEL of 20 mg/kg/day was reported for rats after exposure to trichlorfon based on the modification of immunobiological responses in test animals (Olefir as cited in Zamfir, 1975). A NOEL of 30 mg/kg/day was reported for modification of vitamin metabolism in rats (Nijegoro et al. as cited in Zamfir, 1975), and a NOEL of 57 mg/kg/day was established based on reduced cytochrome oxidase activity in rats (Jdanovici as cited in Zamfir, 1975).

Studies using young dogs as test animals reported a NOEL of 1 mg/kg/day for reduced acetylcholinesterase levels (Jivogliadova et al. as cited in Zamfir, 1975). Decreased levels of acetylcholinesterase in dogs resulted in a higher NOEL of 500 mg/kg in another study (Marsh et al. as cited in Zamfir, 1975). A systemic dog study reported a NOEL of 100 mg/kg based on the modification of intestinal fermentic function upon exposure to higher levels of trichlorfon (Gheorghien as cited in Zamfir, 1975).

Teratology Studies. A teratology study during which pregnant rats were exposed to trichlorfon at the dose level of 8 mg/kg or 80 mg/kg during embryogenesis resulted in malformations and embryotoxicity at the highest dose tested. General edema (accumulation of fluid in body cavities or tissues), hydrocephaly (abnormal increase in cranial fluid), and meningoencephaly (inflammation of the brain and surrounding membranes) were the predominant effects observed in fetuses after exposure to 80 mg/kg of trichlorfon. Based on the absence of terata at 8 mg/kg, the authors suggest that trichlorfon does not pose a danger to humans because the teratogenic dose of 80 mg/kg is 2,500 times the dose likely during a 24-hour exposure period (Marston et al., 1976).

A teratology study during which rats, hamsters, and mice were exposed to trichlorfon during the gestation period resulted in teratogenic effects in all test species. Administration of trichlorfon to rats by gavage during days 6 through 15 of gestation at the dose level of 480 mg/kg/day (lowest effect level) resulted in malformed fetuses. Embryotoxicity and terata were observed in hamsters at the dose level of 400 mg/kg/day. Fetotoxicity characterized by low weight was observed in mice at the dose level of 400 mg/kg/day, and terata reported as the occurrence of cleft palates were reported at 500 mg/kg (Staples et al., 1979).

Mutagenicity Studies. Inconsistent results have been reported from various nonmammalial assays examining the mutagenic potential of trichlorfon in bacteria, fungi, plants, and insects. Trichlorfon was negative in four assays using bacteria cells, while 3 other bacterial assays were reported to be positive for mutagenicity (IARC, 1983). The mutagenic effects observed in bacterial cells were characterized by incorrect substitution of bases in the genetic code. Three mutagenicity assays in fungal systems resulted in the stimulation or induction of mutagenic effects during the process of cell division (mitosis) (IARC, 1983). Insect studies using the fruit fly (Drosophila melanogaster) were negative upon exposure to trichlorfon (IARC, 1983). Chromosome damage was observed in the plant Hordeum vulgare after exposure to trichlorfon (IARC, 1983).

The majority of tests using mammalian cell systems have resulted in positive mutagenic effects. Mutagenic effects were induced in assays examining the mutagenic potential of trichlorfon using hamster cells (CHO), and cells derived from the immune circulatory system and bone marrow of mice (IARC, 1983).

Mutagenicity or the induction of unscheduled DNA synthesis was observed after exposure of two human cell lines (epithelioid and fibroblasts) to trichlorfon (IARC, 1983).

Trichlorfon was nonmutagenic in a dominant lethal mouse assay (Becker et al., 1980).

Oncogenic Studies. A 90-week oncogenic study during which rats were exposed to trichlorfon at a dose of 1.98 g to 2.08 g by oral intubation or intraperitoneal application of 1.1 g to 1.6 g reported that no statistically significant carcinogenic activity was observed in test animals (Mobay, 1979a). A 73- to 75-week oncogenic study during which mice were exposed to trichlorfon at dose levels of 154 to 157.5 mg by oral intubation, 149.7 mg to 160.8 mg by intraperitoneal application, or 375 mg by dermal treatment

did not result in a statistically significant occurrence of benign or malignant tumors (Mobay, 1979b).

CLARIFICATION OF CANCER POTENCIES AND RISKS

This section clarifies and recalculates the cancer potency for N-nitrosocarbaryl, and it clarifies the cancer potency for 4-chloroaniline, a breakdown product of diflubenzuron. This section also clarifies cancer risks.

Carbaryl (N-nitroso-carbaryl)

In addition to the Eisenbrand et al. (1976) study analyzed in Appendix F, two other studies could be used to calculate the potency of N-nitrosocarbaryl: Lijinsky and Taylor (1976) and Lijinsky and Schmahl (1978). These studies used Sprague-Dawley rats force fed N-nitrosocarbaryl by the gavage method of dosing. The results of the studies are listed below:

Reference	Total dose	Sex	Days in lifetime	Animals with cancer (percent)
Lijinsky and Taylor (1976)	50 mg	F	840	75
	300 mg	M	700	47
Eisenbrand et al. (1976)	5,000 mg/kg	M	167	29
Lijinsky and Schmahl (1978)	600 mg/kg	M	630	21
	600 mg/kg	F	840	57

As discussed previously in this appendix (in the subsection on N-nitrosocarbaryl formation), all reported incidences of cancer were tumors of the forestomach, the dosing site of the gavage method. The studies by Eisenbrand et al. (1976) and Lijinsky and Schmahl (1978) reported 10 and 0 percent cancer, respectively, in the control. The Lijinsky and Taylor (1976) study only had a colony control (zero incidence of cancer). For this analysis we will assume that α, the spontaneous cancer rate, is zero because the cancers noted in the control by Eisenbrand et al. (1976) were different from those caused by the treatment.

The average daily dose (d) was calculated by dividing the total dose by the average time of exposure or lifetime (whichever was longer). It also was assumed that, over the duration of the studies, the female rats weighed an average of 0.1 kg and the males weighed 0.2 kg.

Reference	Sex	Average daily dose (mg/kg/day)
Lijinsky and Taylor (1976)	F	0.59
	M	2.41
Eisenbrand et al. (1976)	M	29.94
Lijinsky and Schmahl (1978)	M	0.95
	F	0.71

The cancer potency, β, was calculated from the linear model by solving for β.

$$R = \alpha + d$$
$$\beta = (R - \alpha)/d$$
$$\beta = R/d \text{ where } \alpha = 0.0$$

Using the Eisenbrand et al. (1976) data for example:

$$\beta = R/d = 0.29/29.94 \text{ mg/kg/day}$$

$$\beta = 0.0097 \text{ (mg/kg/day)}^{-1}$$

Other cancer potencies are:

Reference	Sex	Average dose (mg/kg/day)	Incidence	β(mg/kg/day)$^{-1}$
Lijinsky and Taylor (1976)	F	0.59	0.75	1.3
	M	2.14	0.47	0.22
Eisenbrand et al. (1976)	M	29.94	0.29	0.010
Lijinsky and Schmahl (1978)	M	0.95	0.21	0.22
	F	0.71	0.57	0.80

Extrapolating the cancer potency from rats to humans was done by multiplying by the 1/3 power of the ratio of adult human (70 kg) to adult rat (0.35 kg) weights. For example, using the Lijinsky and Taylor (1976) data for female rats, the cancer rate for humans was computed as follows:

$$\beta \text{ (human)} = 1.3 \text{ (mg/kg/day)}^{-1} \times (70/0.35)^{1/3}$$
$$= 7.6 \text{ (mg/kg/day)}^{-1}$$

Cancer potencies for humans from the three studies are estimated below:

Reference	Sex	β Human $(mg/kg/day)^1$
Lijinsky and Taylor (1976)	F	7.6
	M	1.2
Eisenbrand et al. (1976)	M	0.06
Lijinsky and Schmahl (1978)	M	1.2
	F	4.7

Therefore, the cancer potency in humans of N-nitrosocarbaryl could range from 0.06 to 7.6 $(mg/kg/day)^{-1}$ depending upon which cancer study was used for the calculation. Using arithmetic average cancer potency values from Lijinsky and Taylor (1976) and Lijinsky and Schmahl (1978), the average cancer potency of N-nitrosocarbaryl would be 3.6 $(mg/kg/day)^{-1}$. The cancer potency calculated from Eisenbrand et al. (1976) was not included in the average because the dose tested caused an abnormally high amount of acute toxicity, thereby lowering the cancer potency.

It is important to remember that N-nitrosocarbaryl poses a cancer risk to humans only when it forms in nature and then persists long enough at the site of attack (stomach) to cause a reaction (cancer). When carbaryl and nitrite were fed directly to rats, no tumors were observed even though doses up to those causing acute toxicity were tested (Lijinsky and Taylor, 1977).

The cancer risk to an individual exposed to realistic or worst case dietary doses of carbaryl from eradication projects is calculated as follows:

$$R \text{ (risk)} = d = 3.6 \text{ (mg/kg/day)}^{-1} \times d$$

For a realistic dose:

$$R = 3.6 \text{ (mg/kg/day)}^{-1} \times 3.56 \times 10^{-8} \text{ mg/kg/day}$$
$$= 1.3 \times 10^{-7} \text{ (or a risk of about one in 10 million).}$$

For worst case:

$$R = 3.6 \text{ (mg/kg/day)}^{-1} \times 4.45 \times 10^{-7} \text{ mg/kg/day}$$
$$= 1.6 \times 10^{-6} \text{ (or a risk of about two in a million).}$$

Cancer risks to an individual exposed to realistic or worst case dietary doses of carbaryl resulting from suppression projects are 2.1×10^{-7} and 2.7×10^{-6}, respectively.

Diflubenzuron (4-chloroaniline)

In the Final Environmental Impact Statement, the risks of cancer were estimated based on secondary reports because the full data from the National Cancer Institute (NCI) study (NCI, 1979) were not available. Since then, the Forest Service has obtained the data and recalculated the risks accordingly.

The NCI conducted 2-year cancer bioassays of 4-chloroaniline in both rats and mice (NCI, 1979). Dietary concentrations of 4-chloroaniline were 0, 250, and 500 ppm for rats, and 0, 2,500, and 5,000 ppm in mice. The only cancerous tumors found that were considered to be related to the 4-chloroaniline treatment were fibromas and sarcomas in the spleen of male rats and hemangiomatous tumors in mice. In both cases, the incidences of these tumors were not significantly greater statistically than those found in untreated control animals. However, the findings were considered suggestive of carcinogenicity because of the rarity of these tumors in the spleens of rats in the colonies maintained at NCI. These cancer incidence data therefore were used to calculate the worst case cancer potency of 4-chloroaniline assuming the incidence rate to be significant.

The incidence of tumors in rats and mice was as follows:

	Dose		Incidence of Cancer		Cancer Potency	
Animal	ppm	mg/kg/day	Males	Females	Males	Females
Rats	0	0	0.05	--	--	--
	250	12.5	0	--	--	--
	500	25	0.20	--	0.034	--
Mice	0	0	0.1	0	--	--
	2,500	375	0.2	0.06	--	--
	5,000	750	0.28	0.19	0.0036	0.0038

The cancer potency, β, was calculated from the linear cancer model

$$R = \alpha + \beta d$$

For example, the cancer potency of male mice was calculated as follows:

$$R = \alpha + \beta d$$
$$0.28 = 0.1 + \beta\ (750\ mg/kg/day)$$
$$= 0.00024\ (mg/kg/day)^{-1}$$

To extrapolate the cancer potency in mice to humans, the cancer potency was multiplied by the 1/3 power of the ratio of human weight (70 kg) to mouse (0.02 kg) weight:

$$\beta\ (Human) = (70/0.02)^{1/3} \times 0.00024\ (mg/kg/day)^{-1}$$

$$= 0.0036\ (mg/kg/day)^{-1}$$

The cancer potency of 4-chloroaniline therefore could range from 0.0036 to 0.034 $(mg/kg/day)^{-1}$ depending upon which animal study was used to predict cancer in man. The arithmetic average for males of 0.019 $(mg/kg/day)^{-1}$ was used for this analysis.

Based on the recently completed cancer bioassays of diflubenzuron, the cancer risk could be considered to be zero (U.S. EPA, 1985a). However, because of the uncertainty about the carcinogenic potential of 4-chloroaniline, there may be some risk of cancer associated with exposure to diflubenzuron.

The theoretical pathways for metabolic breakdown of diflubenzuron in soil, water, plants, and animals were given in the Diflubenzuron Decision Document (U.S. EPA, 1979). Diflubenzuron breaks down into either 4-chlorophenylurea or 2,6-diflurobenzoic acid. The 4-chlorophenylurea can further break down to 4-chloroaniline, which can further degrade to 4-chloroacetanilide. A review of the literature shows that 4-chloroaniline is rarely found in nature. The major metabolites were 4-chlorophenylurea, 2,6-diflurobenzamide, or 2,6-diflurobenzoic acid (see U.S. EPA, 1979, and Nimmo et al., 1984). The principal exceptions were fish and animals, with fish having as high as 60 percent of the total diflubenzuron residue found as 4-chloroaniline (U.S. EPA, 1979). A rapid depletion of the residues in fish was reported in the Diflubenzuron Decision Document, but no data on persistence were given.

Arguably, the cancer bioassays for diflubenzuron also have measured the cancer risk associated with 4-chloroaniline because this metabolite would be present because of any breakdown. However, if a person consumed large amounts of meat or fish containing diflubenzuron, and therefore 4-chloroaniline residues, he or she possibly could be exposed to higher levels of 4-chloroaniline than were fed the mice and rats in the cancer bioassays. Therefore, the risk of cancer associated with this possible exposure was analyzed.

The realistic and worst case doses of diflubenzuron resulting from residues in fish were estimated to be 0.00003 mg/kg/day (0.06 x 0.0004 mg/kg/day x 1.1) and 0.0006 mg/kg/day (0.06 x 0.0051 mg/kg/day x 2.0) on page F-44. If 60 percent of diflubenzuron is broken down to form 4-chloroaniline, the 4-chloroaniline doses would be 0.0000096 mg/kg/day (0.00003 mg/kg/day x 0.6 x 127.6/210.7) for the realistic case and 0.0002 mg/kg/day (0.0006 mg/kg/day x 0.6 x 127.6/210.7) for the worst case. (The value 127.6/210.7 is the ratio of molecular weights.) Since no persistence data are available, it was assumed that 4-chloroaniline residue in the fish would degrade to zero within 60 days.

The average dose over the 60-day period therefore would be 0.0000048 mg/kg/day (realistic) or 0.0001 mg/kg/day (worst case). The realistic lifetime dose of 4-chloroaniline resulting from eradication projects is then:

$d = 0.0000048$ mg/kg/day x 60 days/project x 6 projects/lifetime x 1/25,550 days/lifetime

$d = 6.8 \times 10^{-8}$ mg/kg/day

The worst case average lifetime dose of 4-chloroaniline from eradication projects is:

$d = 0.0001$ mg/kg/day x 60 days/project x 6 projects/lifetime x 1/25,550 days/lifetime

$d = 1.4 \times 10^{-6}$ mg/kg/day

The average lifetime doses resulting from suppression projects were calculated by multiplying the eradication doses by 1.67, which yields 1.1×10^{-7} and 2.3×10^{-6} mg/kg/day for the realistic and worst case, respectively.

The cancer risk to an individual exposed to diflubenzuron, and therefore possibly to 4-chloroaniline, is calculated as follows for the realistic case from eradication projects:

$$R = \beta d = 0.019 \text{ (mg/kg/day)}^{-1} \times 6.8 \times 10^{-8} \text{ mg/kg/day} = 1.2 \times 10^{-9}$$

Cancer risks to an individual for other realistic or worst case doses are presented below:

	Eradication		Suppression	
	Lifetime Dose	Lifetime Cancer Risk	Lifetime Dose	Lifetime Cancer Risk
Realistic	6.8×10^{-8}	1.2×10^{-9}	1.1×10^{-7}	2.2×10^{-9}
Worst case	1.4×10^{-6}	2.7×10^{-8}	2.3×10^{-6}	4.5×10^{-8}

The cancer risk from accidental spills of diflubenzuron were based on the assumption that an individual would eat 0.5 kg of fish taken from the stream in which the chemical was spilled. To evaluate the risk of cancer from an accidental exposure, the single high dose resulting from dermal exposure, water consumption, or fish consumption needs to be expressed in terms of average lifetime dose.

Lifetime Incidences of Cancer Per Acre

To estimate the number of possible incidences of cancer per acre over a lifetime series of applications, the cancer risk is multiplied by the population at risk (14 individuals/acre based on assumptions stated on pages F-64 and F-65 in Appendix F). This translates to the lifetime incidences of cancer per acre for the lifetime number of applications:

Insecticide/ Exposure Scenario	Incidences of Cancer/Acre/Lifetime Suppression (for 10 applications)	Eradication (for 6 applications)
Carbaryl		
Dietary	2.9×10^{-6}	1.8×10^{-6}
Trichlorfon		
Observer and dietary	1.88×10^{-6}	1.12×10^{-6}
Direct and dietary	1.88×10^{-6}	1.12×10^{-6}
Acephate		
Observer and dietary	3.2×10^{-5}	1.97×10^{-5}
Direct and dietary	3.2×10^{-5}	1.97×10^{-5}
Diflubenzuron		
Eating fish/meat	3.2×10^{-8}	1.7×10^{-8}

In a site-specific environmental assessment, total incidences of cancer in the population can be calculated for a single application by dividing incidences of cancer per acre per lifetime by the number of applications (6 or 10) and multiplying by the total number of acres proposed for treatment. For example, for suppression projects, incidences of cancer are calculated as follows (example for carbaryl: 2.9×10^{-6} applications x number of acres treated):

Carbaryl	
Dietary	No. of acres x 2.9×10^{-7}
Trichlorfon	
Observer and dietary	No. of acres x 1.88×10^{-7}
Direct and dietary	No. of acres x 1.88×10^{-7}
Acephate	
Observer and dietary	No. of acres x 3.2×10^{-6}
Direct and dietary	No. of acres x 3.2×10^{-6}
Diflubenzuron	
Eating fish/meat	No. of acres x 3.2×10^{-9}

In other words, there would be less than one incidence of cancer if carbaryl were sprayed on 3 million acres, or if trichlorfon were sprayed on 5 million acres, or if acephate were sprayed on 300,000 acres, or if diflubenzuron were sprayed on 300 million acres.

The risk associated with spraying with carbaryl or acephate is less than one case per 500,000 acres treated. The risk associated with spraying diflubenzuron is about one case per 30 million acres treated. Forest Service records show that during 1981 through 1984, carbaryl has been used on an average of 81,812 acres yearly while trichlorfon has been applied to an average of 160,867 acres, diflubenzuron has been applied to an average of 141,000 acres, and acephate has been used on less than 1,000 acres. Using these acreage numbers, the added risk of cancer from the use of carbaryl would be 0.02 incidences of cancer ($2.9 \times 10^{-7} \times$ 81,812) in the estimated exposed population of 1.14 million people (14 people/acre x 81,812 acres). There would be 0.03 incidences ($1.88 \times 10^{-7} \times 160,867$) of cancer in the estimated exposed population of 2.25 million people (14 people/acre x 160,867 acres) living on the 160,867 acres treated with trichlorfon. These would be 0.0005 incidences

($3.2 \times 10^{-9} \times 141{,}000$) of cancer in the estimated population of 2 million people living on the acres treated with diflubenzuron.

Cumulative Effects

In eradication treatments where a second application of a chemical insecticide is applied 7 to 10 days after the first, exposure levels after the second application will exceed doses discussed under the realistic case for threshold effects for all exposure scenarios. However, the expected realistic exposure level will be less than 2 times the realistic case dose since some degradation of the first application will have occurred before the second one is applied. Expected doses would equal or slightly exceed the ADI for acephate and trichlorfon when dietary components are included (see tables 8 and 11 of Appendix F) but would be lower than the ADI for carbaryl and diflubenzuron (tables 9 and 10 of Appendix F).

The expected worst case exposures under the double application eradication approach likely would exceed the ADI only where dietary components are considered for acephate, carbaryl, and diflubenzuron. Expected worst case exposures for all exposure scenarios involving trichlorfon except indirect would equal or exceed the ADI.

Given the natural spread and subsequent establishment of gypsy moths into areas previously uninfested, it is possible that suppression projects could be conducted in areas that previously received eradication treatments. For example, Tennessee, Michigan, and Oregon have isolated infestations that currently are being controlled through eradication projects. If the eradication efforts fail, the area (or State) could be declared generally infested. In such cases, it then would be possible to be exposed to both eradication (6 exposures) and suppression (10 exposures) projects in a lifetime, for a maximum of 16 exposures.

For threshold effects, these additional exposures will not result in any human health effects that have not already been discussed in the risk analysis. However, the cumulative impact of these additional exposures will increase the weighted lifetime risk of cancer and heritable mutations. Weighted cancer risks are shown in Table I-2, which updates Table 16 of Appendix F.

In all cases the weighted lifetime risk of cancer and heritable mutations are the same order of magnitude as those associated with suppression or eradication projects alone (less than one in a million).

Table I-2.--Weighted risk of cancer in a 70-year lifetime from exposure to acephate, carbaryl, diflubenzuron, or trichlorfon as used in gypsy moth suppression or eradication projects.

Insecticide Exposure Scenario	Weighted Lifetime Cancer Risk		
	Eradication (6 applications)	Suppression (10 applications)	Eradication & Suppression (16 applications)
Acephate			
Direct and dietary	1.4×10^{-6}	2.4×10^{-6}	3.8×10^{-6}
Observer and dietary	1.4×10^{-6}	2.4×10^{-6}	3.8×10^{-6}
Carbaryl (N-nitrosocarbaryl)			
Dietary	1.3×10^{-7}	2.1×10^{-7}	3.4×10^{-7}
Diflubenzuron (4-chloroaniline)			
Dietary	1.2×10^{-9}	2.3×10^{-9}	3.5×10^{-9}
Trichlorfon			
Direct and dietary	8.0×10^{-8}	1.3×10^{-7}	2.1×10^{-7}
Observer and dietary	8.0×10^{-8}	1.3×10^{-7}	2.1×10^{-7}

Accidents

The cancer risks associated with the accident scenarios for trichlorfon, carbaryl, acephate, and diflubenzuron are shown in Table I-3.

Table I-3.--Cancer risks for accidents

Scenario	Realistic	Worst Case
Trichlorfon		
Aircraft Spill		
Dermal (partial)	1.08×10^{-6}	1.95×10^{-6}
Dermal (full)	2.23×10^{-6}	4.05×10^{-6}
Drinking water	6.08×10^{-9}	1.11×10^{-8}
Truck Spill:		
Dermal	1.87×10^{-4}	1.87×10^{-4}
Drinking water	4.18×10^{-8}	4.18×10^{-8}
Carbaryl		
Aircraft Spill		
Drinking water	2.5×10^{-8}	4.5×10^{-8}
Truck Spill		
Drinking water	1.9×10^{-7}	1.9×10^{-7}
Acephate		
Aircraft Spill		
Dermal (partial)	5.7×10^{-6}	1.0×10^{-5}
Dermal (full)	1.2×10^{-5}	2.2×10^{-5}
Drinking water	3.2×10^{-8}	5.9×10^{-8}
Truck Spill		
Dermal	1.0×10^{-3}	1.9×10^{-3}
Drinking water	2.4×10^{-7}	4.4×10^{-7}
Diflubenzuron		
Aircraft Spill		
Eating fish	1.0×10^{-10}	1.8×10^{-10}
Truck Spill		
Eating fish	6.7×10^{-10}	1.2×10^{-9}

CLARIFICATION OF EXPOSURE INFORMATION

This section clarifies the discussion in Appendix F regarding how animals are exposed to the insecticides (see page F-35 and F-36), and the assumptions used to determine oral doses to humans from drinking water containing insecticide residues (see pages F-41 and F-42 of Appendix F).

Animals may be exposed to insecticides as a result of ingesting plant material and water, as well as through grooming. Studies of residues of acephate, carbaryl, and trichlorfon on vegetable crops or grass illustrate that initial residues of insecticides range from 1 to 100 ppm depending on the insecticide and type of the vegetation (see, for example, Pieper, 1979; U.S. EPA, 1983; Back, 1961; and Kuhr and Dorough, 1976). These residues degrade to nondetectable levels within 10 to 14 days on vegetation except for grass, which can have detectable residues for up to 28 days (Pieper, 1979). There are few data available on the persistence of diflubenzuron on vegetation, but there are indications that it persists for a number of months (Wilcox and Coffey, 1978).

The estimated oral doses that result from a person drinking water that contains insecticide residues is based on the following assumptions:

- Direct application of insecticide to water (contrary to normal operating procedures)

- Water sources will have a minimum average depth of 6 inches.

- Realistic insecticide concentrations are 50 ppb (0.05 mg/liter) for every 1 lb. a.i. per acre application. Worst case concentrations are 0.707 mg/liter for every 1 pound a.i. per acre application of insecticide.

- Daily consumption of water is 2 liters.

- Water consumed is from a surface spring or stream that had direct application.

- Actual persistence times depend on many environmental factors, but data from gypsy moth projects indicate that residues do not remain in running water for more than 2 to 6 days (see, for example, LOTEL, 1975, and Pieper, 1979). Persistence can be much longer in stagnant water bodies (Gibbs et al., 1984), but these are much less likely sources of drinking water.

- It is possible that after spray application, some insecticide might be dislodged by rain within 10 days (based on half-life data) (FEIS, Table 2), and runoff into potable water. This may result in a brief increase in the concentration of insecticide in water. The transitory nature of these residues and the relatively small contribution of drinking water to human exposure compared to the dermal exposure values already estimated (p. F-32) indicate that runoff is not a significant contribution factor for exposure and is thus not considered in this analysis.

ERRATA

The corrections listed in this section should be made to the main text and to Appendix F of the 1985 Final EIS.

Page 6 - In paragraphs 3 and 4, change references from "EPA 1975" to "USDA, 1981a." The reference USDA (1981a) provides more current information.

Page 11 - In third listed item, delete "(Atherton 1977)" reference. This reference is unnecessary.

Page 18 - In paragraph 5, last sentence, add "(1981)" after "Atkins et al." and change "highly toxic" to "relatively nontoxic." These changes correct the citation. The sentence should now read as follows:

Based on work by Atkins et al. (1981), EPA concluded that Sevin XLR is relatively nontoxic to honeybees exposed to direct application.

Page 22 - In paragraph 2, last line, change reference from "PA Bureau of Forestry 1983" to "PA DER, 1983." This change corrects the citation.

Page 32 - In paragraph 6, line 5, delete reference to "Kondakov 1963." This reference is one of several and is extraneous.

Page 43 - In second line on page, change reference from "Wilcox (1973)" to "LOTEL (1975)." The LOTEL (1975) reference provides updated information.

Page 44 - In paragraph 3, line 7, change reference from "Zinkl et al. 1979" to "Zinkl et al., 1980." The reason for this change is that Zinkl et al. (1980) provides updated information.

Page 49 - In paragraph 1, line 4, delete "(USDA 1968)" reference. This reference is extraneous.

Page 50 - In paragraph 4, line 3, change reference from "Union Carbide 1969" to "Dolinger and Fitch, undated." Dolinger and Fitch (undated) provides updated information.

Page 50 - In paragraph 5, line 5, change reference from "Johansen (1959)" to "Atkins et al. (1981)." Atkins et al. (1981) provides updated information.

Page 53 - In paragraph 2, line 2, change reference from "Zinkl et al. (1979)" to "Zinkl et al. (1980)." Zinkl et al. (1980) provides updated information.

Page 53 - In paragraph 4, delete "by the South Carolina Epidemiologic Studies Center (1979)" and add "(USDA 1981c)" to end of paragraph. These changes correct the citation. The sentence should now read as follows:

In forest openings, actual dermal exposure studies conducted during Maine's spruce budworm spray project showed a total dermal exposure of 10 mg carbaryl for a person (150 pounds) who is 80 percent clothed at the time of application (USDA, 1981c).

Page 53 - In paragraph 6, line 7, change reference from "SCESC 1978" to "SCESC, 1979a." This change corrects the citation.

Page 55 - In second indented paragraph, last line, delete "not." This change corrects the quotation. The sentence should now read as follows:

Alpha-naphthol residues in the residential participants indicated that drift did occur.

Page 55 - In paragraph 1 (first paragraph following indented quotation), last line, change reference from "SCESC 1979" to "SCESC, 1979a, 1979b." This change corrects the citation.

Page 56 - In paragraph 3, first line, change reference from "SCESC 1978, 1979" to "SCESC, 1979a, 1979b." This change corrects the citation.

Page 60 - In paragraph 3, line 17, change reference from "Lijinsky and Taylor 1977" to "Lijinsky and Taylor, 1976." This change corrects the citation.

Page 61 - In paragraph 5, delete sentence 4. The reason for this deletion is that a new label was approved by EPA in April 1985 that expands previous site restrictions.

Page 62 - In paragraph 6, lines 3 and 4, delete "Steelman et al. 1975" reference. The reference is one of several and is extraneous.

Page 64 - In paragraph 3, line 4, delete "Abdalla et al. 1965" reference. The reference is one of several and is extraneous.

Page 64 - In paragraph 3, line 7, change reference from "EPA 1969" to "Meister, 1983." The reason for this change is that Meister (1983) provides updated information.

Page 65 - In paragraph 4, line 3, delete "Pearce 1970" reference. The reference is one of several and is extraneous.

Page 65 - In paragraph 4, line 9, change reference from "Johansen 1959" to "Atkins et al., 1981." The reason for this change is that Atkins et al. (1981) provides updated information.

Page 69 - In paragraph 7, delete first sentence. This statement was inadvertently carried forward from a working draft and is extraneous.

Page 85 - Delete the following references because they are no longer cited in the text:

Abdalla et al., 1965.

Atherton, 1977.

Page 85 - Insert the following references:

Abrahamsen, L. H. and M. Jerkofsky.
1981. Enhancement of varicella-zoster virus replication in cultured human embryonic lung cells treated with pesticide carbaryl. App. Environ. Microbiology 41(3): 652-656.

Brookman, D. H., C. Chopna, D. J. Ecobichon, C. Y. Kana, L. Ritter, and J. Thorsen.
1984. Assessment of the potential of insecticides, emulsifiers, and solvent mixtures to enhance viral infection in cultured mammalian cells. App. Environ. Microbiology 47(1): 80-83.

Page 86 - Delete the following reference because it is no longer cited in the text:

Chemagro, 1968.

Page 86 - Change title of Chevron Chemical Co., 1973, from "Orthene insecticide--environmental impact report" to "The impact of orthene on the environment."

Page 86 - Change report number of Chevron Chemical Co., 1975, from "75238-13-2/75" to "75238-13-R1 10-75."

Page 87 - Delete the following references because they are no longer cited in the text:

Environmental Protection Agency, 1969.
Environmental Protection Agency, 1975.

Page 87 - Change authors of Doane and Hitchcock, 1964, from "Doane, C. C. and J. W. Hitchcock" to "Doane, C. C. and S. W. Hitchcock."

Page 87 - Insert the following reference:

Elespuru, R., W. Lijinsky, and J. Setlow.
1974. Nitrosocarbaryl as a potent mutagen of environmental significance. Nature 247:386-387.

Page 88 - Delete the following reference because it is no longer cited in the text:

Fishbein, 1978.

Page 89 - Delete the following reference because it is no longer cited in the text:

Innes, et al, 1969.

Page 89 - Change title of Heimpel, 1971, from "Safety of insect pathogens (in man and vertebrates)" to "Safety of insect pathogens for man and vertebrates."

Page 90 - Delete the following references because they are no longer cited in the text:

Johansen, 1959.
Kondakov, 1963.

Page 91 - Delete the following reference because it is no longer cited in the text:

Marston and Voronina, 1976.

Page 91 - Insert the following reference:

Lijinsky W. and C. Winter.
1981. Skin tumors induced by painting nitrosoalkylureas on mouse skin. J. Cancer Res. and Clin. Oncol. 102:13-20.

Page 92 - Delete the following reference because it is no longer cited in the text:

Pearce, 1970.

Page 93 - Change authors of Richmond et al., 1979, from "Richmond, M. L., C. J. Henny, R. L. Floyd, R. W. Marnan. D. M. Finch, and L. R. DeWeese." to "Richmond, M. L., C. J. Henny, R. L. Floyd, R. W. Mannan, D. M. Finch, and L. R. DeWeese."

Page 93 - Insert the following reference:

Schmidt, N.
1983. Effect of the pesticide carbaryl on replication of human and simian varicella viruses. Infection and Immunity 39(3): 1485-1487.

Page 94 - Delete the following references because they are no longer cited in the text:

Staples et al., 1976.
Steelman et al., 1975.

Page 94 - Change date and title of SCESC, 1978, from "1978. Measure of exposure to the carbamate carbaryl: Maine carbaryl study, 1978" to "1979a. Measurement of exposure to the carbamate carbaryl: Maine carbaryl study, 1978."

Page 94 - Change date and title of SCESC, 1979, from "1979. Measure of exposure to the carbamate carbaryl: Maine carbaryl study, 1979" to "1979b. Measurement of exposure to the carbamate carbaryl: Maine carbaryl study, 1979."

Page 95 - Delete the following reference because it is no longer cited in the text:

U.S. Department of Agriculture, 1968.

Page 95 - Change the booklet number of Union Carbide, 1968, from "IOG-0049A" to "ICG-0449A."

Page 96 - Delete the following reference because it is no longer cited in the text:

U.S. Department of Agriculture, 1983.

Page 96 - Change title and report number of Wegner, 1970, from "Bilarcil (R) (Bay 2349) clinical trials 1960-1969 . . . . Rept. 225" to "Bilarcid (R) (Bay 2349) clinical experience 1960-1969. . . . Rept. 2225."

Page 96 - Insert the following reference:

U.S. Department of Agriculture.
1981c. Final programmatic EIS, proposed cooperative 5-year (1981-1985) spruce budworm management program for Maine. Northeastern Area State and Private Forestry, Feb. 12, 1981.

Page 97 - Delete the following references because they are no longer cited in the text:

Wilcox, 1973.
Zinkl et al., 1979.

Page F-38 - In paragraph 2, change last word of line 7 from "of" to "or." The sentence should now read as follows:

Also, applications of 0.7 lb a.i. acephate/acre in New York (LOTEL 1975) resulted in non-detectable levels (less than 0.05 ppm) of acephate in the liver or muscle tissue of rodents trapped in the treated area.

Page F-122 - In Table 7, change the carcinogenic potency for trichlorfon from "0.047" to "0.0047." This change corrects a typographical error.

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